

Twin pregnancy outcome among cases of spontaneous conception, intrauterine insemination, and in vitro fertilization/intracytoplasmic sperm injection

In a retrospective university hospital-based study of spontaneously conceived (SC), intrauterine insemination (IUI), and in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) groups, this study finds maternal complications or the neonatal outcomes of twins to be similar between the groups. (*Fertil Steril*® 2006;86: 1017–9. ©2006 by American Society for Reproductive Medicine.)

With assisted reproductive technologies (ARTs) now being more frequently performed, a corresponding increase in the number of multiple pregnancies has occurred (1). Many of the prior studies comparing spontaneous conception (SC) and ART have demonstrated that ARTs gave rise to detrimental effects for both mothers and neonates (2–4). In contrast to the classifications adopted in much of the prior research in this area, our study takes the step of classifying twins into three distinct groups: SC, intrauterine insemination (IUI), and in vitro fertilization/intracytoplasmic sperm injection–embryo transfer (IVF/ICSI-ET). The main purpose for this clear classification in cases of twin pregnancies is to facilitate further observation to determine whether IUI or IVF/ICSI-ET are similar to those conceived spontaneously.

This study examines a total of 240 twin births delivered at the Taipei Medical University Hospital, a tertiary referral hospital with high-risk cases, during the period 1992–2001, excluding from the sample all patients with any prior history of hypertension or diabetes mellitus. Abortions, fetuses with a birth age of <24 gestational weeks, and higher-order multiple births were also excluded. The final exclusion criterion involved those cases with incomplete data, or those that were lost in follow-up. A total of 46 patients were ultimately excluded, leaving 194 patients as the total sample for this study; these were then divided into three groups: SC (n = 50), IUI (n = 63), and IVF/ICSI (n = 81).

These 194 patients were all observed regularly in our obstetrics outpatient department, with comparisons being made between maternal complications, including preterm labor, premature rupture of the membrane (PROM), pregnancy-induced hypertension (PIH), gestational diabe-

tes mellitus (GDM), postpartum hemorrhage (PPH) and maternal mortality. Postpartum hemorrhage was defined in this study as hemorrhaging >1000 mL following delivery.

A total of 388 neonates were analyzed from the aspects of incidence of preterm birth, stillbirth rate, birth weight, Apgar scores, neonatal morbidity, and mortality rates, with all statistical analyses being performed using the Statistical Package for the Social Sciences (SPSS) version 10.0 (SPSS Inc., Chicago, IL). One-way analysis of variance (ANOVA), post hoc test, and χ^2 analyses were used to evaluate the differences among the three groups for continuously distributed and categorical variables, respectively, with a value of $P < .05$ considered significant. Approval for this study was obtained from the Institutional Review Board at the Taipei Medical University Hospital.

The results are listed in Table 1. Among the three groups in this study, the mean maternal age (mean \pm SE) at delivery was 31.8 ± 3.7 years for SC; 32.1 ± 3.0 years for IUI; and 33.7 ± 4.6 years for IVF/ICSI ($P = .011$). The rates of PROM were 18.0% for the SC group, 3.2% for the IUI group, and 13.6% for the IVF/ICSI group ($P = .034$). The incidences of preterm labor, PIH, GDM, preterm birth, and the mean gestational ages among the three groups were all similar.

Cesarean section rates were 74.0% for the SC group, 90.5% for the IUI group, and 95.1% for the IVF/ICSI group ($P < .001$), whereas the respective mean blood losses at delivery were 504 ± 224 mL; 662 ± 684 mL; and 624 ± 442 mL ($P = .227$). Placenta abruption occurred in 1 of 63 cases in the IUI group, whereas placenta accreta occurred in 1 of 81 in the IVF/ICSI group, but neither complication was present in the SC group. There were four cases (6.3%) of placenta previa in the IUI group, and an additional four cases (4.9%) in the IVF/ICSI group, but no cases were present in the SC group ($P = .215$). Postpartum hemorrhage occurred in 8% of cases in the SC group, 14.3% in the IUI group, and 9.9% in the IVF/ICSI group ($P = .530$). One mother in the IVF/ICSI group died of disseminated intravascular coagulation derived from PIH and PPH.

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TABLE 1

Maternal complications and neonatal outcomes of twins, by SC, IUI, and IVF/ICSI groups

	SC (n = 50)	IUI (n = 63)	IVF/ICSI (n = 81)	P value
Maternal age (y) (mean ± SE)	31.8 ± 3.7	32.1 ± 3.0	33.7 ± 4.6	<.05
Preterm labor (%)	30.0	25.5	32.1	.408
Premature rupture of membrane (%)	18.0	3.2	13.6	<.05
Pregnancy-induced hypertension (%)	8.0	7.9	12.3	.599
Gestational diabetes mellitus (%)	4.0	0.0	6.2	.141
Placenta abruption (%)	0.0	1.6	0.0	.352
Placenta accreta (%)	0.0	0.0	1.2	.496
Placenta previa (%)	0.0	6.3	4.9	.215
Cesarean sections (%)	74.0	90.5	95.1	<.001
Mean blood loss at delivery (mL)	504 ± 224	662 ± 684	624 ± 442	.227
Postpartum hemorrhage (%)	8.0	14.3	9.9	.530
Maternal death (%)	0.0	0.0	1.3	.496
Preterm birth (<32 weeks) (%)	6.0	3.2	6.2	.786
Preterm birth (<37 weeks) (%)	40.0	36.5	43.2	
Term birth (≥37 weeks) (%)	54.0	60.3	50.6	
Gestational age (wks)	36.4 ± 2.8	36.2 ± 2.4	36.0 ± 2.3	.647
Very low birth weight (≤1,500 g) (%)	7.0	6.3	5.6	.891
Low birth weight (≤2,500 g) (%)	37.0	46.0	48.0	.345
Birth weight (g)	2,434 ± 58	2,359 ± 46	2,407 ± 40	.548
Mild depression (%) ^a	11.0	9.5	11.1	.898
Severe depression (%) ^b	1.0	1.6	3.7	.296
Stillbirth (%)	5.0	2.4	1.2	.200
Neonatal morbidity (%)	13.0	15.9	19.8	.346
Neonatal mortality (%)	3.0	0.8	0.6	.210

Note: n = number of twin-pregnant cases (mean ± SE).

^a Mild depression refers to an Apgar score at 1 minute of <7, and at 5 minutes of ≥7.

^b Severe depression refers to an Apgar score at 5 minutes of <7.

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The incidences of stillbirth, neonatal depression, very low birth weight, low birth weight (LBW), and mean birth weights were not significantly different. The neonatal morbidity rates (i.e., the neonatal intensive care unit admission rate) were 13.0% for the SC group, 15.9% for the IUI group, and 19.8% for the IVF/ICSI group, whereas the respective neonatal mortality rates were 3.0%, 0.8%, and 0.6%. In summary, this study finds the morbidities for mother and neonate to be similar among the groups.

With regard to maternal pregnancy outcomes, we can find no discernible differences among the three groups, with the exception of the higher cesarean rates in both the IUI and IVF/ICSI groups, as compared with the SC group. These higher cesarean rates in the former groups are responsible for consuming greater medical expenses (5, 6). We find that there are virtually no other disadvantages to the mother that might be attributable to ARTs.

According to our data, there was a lower incidence of PROM in the IUI group as compared with the other two groups ($P=.034$). In a review of the prior studies, there

appears to have been no mention of such a phenomenon in the case of twin pregnancies, although one study did find that IUI did not contribute to a lower incidence of PROM in single pregnancies (7). We postulate that a possible reason for this phenomenon is our limited sample size, and therefore suggest that a larger, prospective, randomized, controlled, multicentered trial will be required to further verify the current data.

As for neonatal outcomes, although Zuppa et al. (3) argued that assisted twin pregnancies led to higher incidences of preterm birth, fetal depression at birth, LBW, and neonatal morbidity in neonates ($n = 32$), as compared with those from SC twin pregnancies ($n = 228$), we do not find their results so convincing because of the smaller ART population examined in their study. In comparative terms, the present study has produced totally different results. Our data, comprising 388 neonates, was divided into three groups: SC ($n = 100$), IUI ($n = 126$), and IVF/ICSI ($n = 162$), with many aspects of these cases being analyzed. Our results demonstrate no significant differences among the three groups, not only in terms of

incidences of preterm birth, fetal depression, LBW, and neonatal morbidity, but also in terms of the rate of stillbirths and neonatal mortality.

To our knowledge, this is the first twin pregnancy study that has divided ARTs into two groups: IUI and IVF/ICSI-ET. Our intention was to evaluate which ART causes adverse maternal and fetal outcomes as compared with SC; however, to our surprise, this study finds maternal complications and neonatal outcomes to be similar between the groups. We believe, therefore, that the clear distinctions reported in some of the prior studies deserve careful thought and much further research. Most of the prior studies failed to make any clear mention of the IUI categories, whereas some even grouped IUI with SC (3–6, 8). In our opinion, based on these vague, perhaps even confusing categorizations, the poor maternal and fetal outcomes attributed to ART have yet to be proven.

Although IUI and IVF/ICSI do contribute to high cesarean rates in twin pregnancies, and thereby higher medical costs, they appear to have had no major detrimental effects on either maternal or fetal outcomes compared with SC. Indeed, the results of our research are similar to the findings of recent studies by Luke et al. (9), which indicated that assisted conception did not represent a risk factor in terms of an association with adverse outcomes in twin pregnancies.

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