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MATERNAL-FETAL MEDICINE

Obstetrical outcomes of embryo reduction and fetal reduction compared to non-reduced twin pregnancies

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Abstract

Purpose To prevent perinatal morbidity and mortality of high-order multiple pregnancy (HOMP), multifetal pregnancy reduction (MPR) is offered to some patients. In this study, we investigated whether twin pregnancies derived from MPRs carry a higher adverse obstetrical outcome compared to non-reduced control group of twins.

Methods We retrospectively analyzed the data from HOMPs on which transvaginal ER ($n=153$) at a mean gestational age of 7.6 weeks or transabdominal FR ($n=59$) at a mean gestational age of 12.4 weeks was performed between December 2006 and January 2018. The risk of each procedure was evaluated by comparing obstetrical outcome with that of a control population of 157 non-reduced twins conceived by infertility treatment.

Results The mean gestational ages at delivery were 35.2 weeks in the ER group, 35.7 weeks in the FR group, and 34.1 weeks in the control group (P = NS). Compared with those in the control group, the ER group had higher miscarriage (1.3% vs. 6.5%; $P=0.047$; OR 0.21; 95% CI 0.45–0.898) and higher overall fetal loss (3.8% vs. 14.4%; $P=0.003$; OR 0.24; 95% CI 0.09–0.60) rates. Differently compared with those in the control group, the FR group had no statistical difference in miscarriage (2.5% vs. 1.7%; P=NS) and overall fetal loss (3.8% vs. 6.8%; P=NS) rates.

Conclusions Compared with the control group, ER in twins had a higher miscarriage and fetal loss rate, whereas FR in twins was similar to the control group. So, the FR procedure is overall a better and safer approach of MPR in reducing morbidity and mortality in HOMPs.

Keywords High-order multiple pregnancies · Multifetal pregnancy reduction · Twin pregnancy · Miscarriage rate · Preterm delivery

Introduction

The incidence of high-order multifetal pregnancies (HOMPs, i.e., more than twins) has risen over the years due to increased likelihood of infertility and the need for artificial reproductive technology (ART) use due to delayed childbearing [1]. We are aware that HOMPs increase perinatal morbidity and mortality due to prematurity. Recent data suggests that risks of preterm delivery under 32 weeks' gestation and of birth weight at delivery under 1500 g were shown to be threefold higher for triplet pregnancies compared with twins [2, 3]. To prevent fetal loss, preterm delivery, and perinatal morbidity in HOMPs, multifetal pregnancy reduction (MPR) is offered to some patients [4].

MPR is defined as a first-trimester or early second-trimester procedure for reducing the total number of fetuses in HOMPs by one or more [1]. Two different MPR methods performed under ultrasonographic guidance are practiced, namely, transvaginal ultrasound-guided embryo reduction (ER), which is performed at between 6 and 8 weeks of gestation, and transabdominal ultrasound-guided fetal reduction (FR), which is performed after 11 weeks of gestation [5]. The safety of MPR is a crucial issue for both the parents and physicians, and especially for those couples that have achieved a pregnancy following ART. While studies have investigated the obstetrical outcomes associated with each

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procedure individually or MPR as whole [6], insufficient data, however, are only available on comparing the two techniques with the control group.

It has been shown that twin pregnancies conceived by ART resulted in an increased risk of some neonatal complications, compared to spontaneously conceived twins [7–9]. Because all ER and FR cases were conceived by ART, it was thought to be clearer to compare the outcomes with the ART-conceived twins. Therefore, in this study, we excluded spontaneously conceived pregnancies.

The aim of the present study was to compare the obstetrical outcomes that followed transvaginal ER or transabdominal FR in twin pregnancy and to compare with non-reduced twins.

Methods

From December 2006 to January 2018, MPRs in twins were performed at the Fertility Center and at the Department of Obstetrics and Gynecology, CHA Bundang Medical Center, CHA University, Seongnam, Republic of Korea. The exclusion criteria were undergoing MPR twice, or a remaining fetus with a known chromosome anomaly or lethal anatomical defect. After exclusion, 212 patients were included in the study. ER was performed by two of the authors at the Fertility Center on 153 patients whose gestational ages were between 6 and 8 weeks (Group 1). FR was performed after sonographic fetal anomaly scans according to the guidelines [10] and, if needed, chorionic villus sampling (CVS), by one of the authors at the Department of Obstetrics and Gynecology on 59 patients whose gestational ages were between 11 and 17 weeks (Group 2). To evaluate effects of ER and FR on clinical outcomes, cases were compared with 157 control series of dichorionic-diamniotic twins conceived by infertility treatment (Group 3).

A transvaginal approach was used for ER. Under ultrasound visualization, a 17-gauge needle was inserted through the internal cervical os and directed towards the sac. Hand suction was used to aspirate the fluid and fetus from the sac. The criteria for the selection of the fetus (es) were ranked as follows: monochorionic twins, a fetus with a weak heartbeat, a shorter than expected crown-rump length or a smaller than expected gestational sac, and if all of these were normal, the easiest fetus to approach.

FR was performed transabdominally. Under the guidance of an abdominal ultrasound transducer, a 22-gauge needle was inserted into the uterine cavity and into the fetal heart or thoracic cavity, an intracardiac or intrathoracic injection of potassium chloride was administered, and the fetal heart was monitored visually for asystole. The criteria for the selection of the fetus (es) were ranked as follows: those with anatomical defects, including an enlarged nuchal translucency, chromosomal anomalies detected by chronic villus sampling, and if these were normal, the easiest fetus to approach. No hormonal supports or antibiotics were used during ER and FR.

The data were collected retrospectively at the Fertility Center and the Department of Obstetrics and Gynecology following CHA Bundang Medical Center institutional review board approval (2018-03-017). The baseline characteristics were analyzed, including the conception mode, gestational age at the time of MPR, history of miscarriage (< 24 weeks' gestation) or preterm delivery (< 34 weeks' gestation), and history of loop electrosurgical excision procedure (LEEP) or myomectomy. The conception modes were defined as achieved through ART, or through intrauterine insemination. The indications for MPR were HOMPs which include triplets and above. The obstetrical outcomes assessed in this study included the miscarriage rate, which was defined as a delivery at ≥ 12 and < 24 weeks' gestation, early and late preterm deliveries, defined as a delivery at ≥ 24 weeks and < 34, ≥ 34 and < 37 weeks, term delivery, maternal complications, and fetal loss, which was defined as the loss of one or two fetuses during pregnancy. The mean birth weight and the need for neonatal intensive care unit (NICU) admission were also recorded.

The statistical analyses were performed using the IBM®SPSS® software, version 24 (IBM Corporation, Armonk, NY, USA). The statistical significance of the differences between the ER group, FR group and control group was analyzed using the one-way ANOVA and χ^2 test, and a two-tailed unpaired Student's *t* test, as appropriate. Logistic regression analysis was used for the multivariate analysis while controlling for the effects of the potential confounders, which included the maternal age, body mass index, parity, mode of conception, and maternal histories. Kaplan–Meier curves were generated for GA at delivery by different MPR procedures with control group and compared using the log-rank test. A value of $P < 0.05$ was considered significant.

Results

A total of 287 patients who underwent MPR in twins were evaluated. Excluding 72 patients of incomplete follow-up, one case with anatomical anomaly (suspected Ebstein anomaly after ER), and two cases which underwent MPR twice (suspected with pentalogy of Cantrell at 11–15 gestational weeks after ER and underwent FR), a total of 212 patients were included in this study (Fig. 1), i.e., 153 patients who underwent ER (Group 1), 59 patients who underwent FR (Group 2), and 157 patients in the control group. Table 1 presents the study population's characteristics. Significant differences were noted in maternal age and history of preterm delivery. No clinical or statistical significance was found

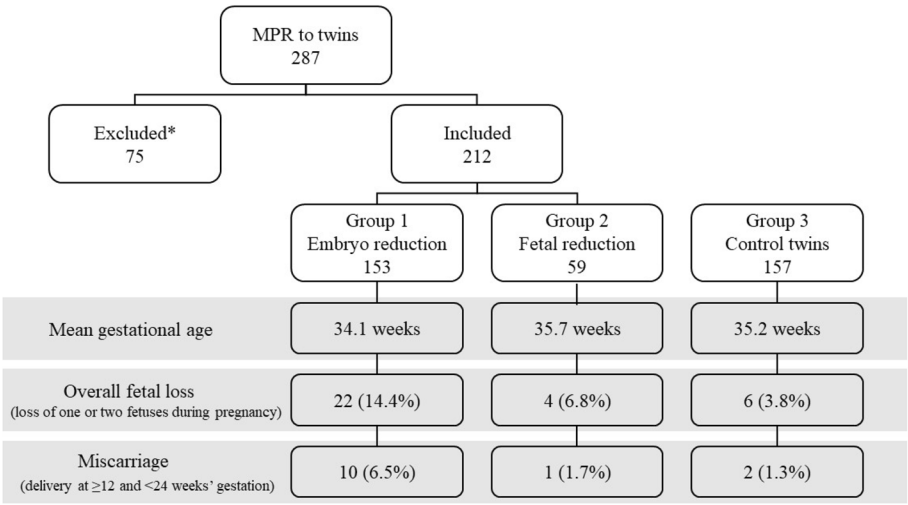

Fig. 1 Flow chart of the study population

Table 1 Baseline characteristics

	Group 1, embryo reduction ($n=153$)	Group 2, fetal reduction ($n=59$)	Group 3, control twins ($n=157$)	p value
Age (years)	33.0 ± 3.5	32.5 ± 3.7	33.9 ± 3.0	0.011
Weight (kg)	57.4 ± 10.6	56.2 ± 10.5	59.1 ± 9.7	0.131
Body mass index (kg/m^2)	21.9 ± 3.7	21.6 ± 3.6	22.2 ± 4.0	0.550
Nulliparity	132 (86.3%)	50 (84.7%)	142 (90.4%)	0.392
Multiparity	21 (13.7%)	9 (15.3%)	15 (9.6%)	0.392
Conception mode, IUI	16 (10.5%)	6 (10.2%)	20 (12.7%)	0.778
Conception mode, IVF/ICSI	137 (89.5%)	53 (89.8%)	136 (86.6%)	0.673
Hx. of miscarriage	0 (0%)	1 (1.7%)	1 (0.6%)	0.314
Hx. of preterm delivery	0 (0%)	2 (3.4%)	0 (0%)	0.005
Hx. of LEEP	0 (0%)	2 (3.4%)	5 (3.2%)	0.080
Hx. of myomectomy	6 (3.9%)	2 (3.4%)	5 (3.2%)	0.938
Mean gestational age at the time of the procedure (weeks)	7.6 ± 0.4	12.4 ± 0.9	–	< 0.001
Mean number of embryos, initial	3.2 ± 0.6	3.3 ± 0.5	–	0.883

Data are represented as mean value ± standard deviation or n (%)

IUI intrauterine insemination, *IVF/ICSI* in vitro fertilization by intracytoplasmic sperm injection, *Hx* history, *LEEP* loop electrosurgical excision procedure

regarding other backgrounds. The mean gestational ages at which the procedures were undertaken were 7.6 weeks for Group 1 and 12.4 weeks for Group 2 ($P<0.001$). Group 1 and Group 2 had a similar proportion of MPR indication of triplets (81% vs. 78%, P = NS) and above triplets (19% vs. 22%, P = NS).

Kaplan–Meier curves were generated for GA at delivery by MPR procedures and compared using the log-rank test showing significant difference between Groups 1 and 3 ($P=0.003$) (Fig. 2) and between Groups 2 and 3 ($P=0.046$) (Fig. 3). The obstetrical outcomes are presented in Table 2 and Fig. 1. After adjusting for the potential confounders described previously, the overall fetal loss rate was significantly higher in Group 1 (14.4%) compared with that in Group 3 (3.8%) ($P=0.003$) [odds ratio (OR), 0.24; 95% confidence interval (CI) 0.09–0.60] and the miscarriage rate was also significantly higher in Group 1 (6.5%) compared with that in Group 3 (1.3%) ($P=0.047$) (OR 0.21; 95% CI 0.45–0.98). However, Group 2 and 3 did not differ with respect to overall fetal loss and the miscarriage rate. The mean gestational age of delivery was 34.1 ± 6.4 weeks in Group 1, 35.7 ± 2.5 weeks in Group 2, and 35.2 ± 4.0 weeks in Group 3 without significant difference. After adjustment, frequencies of incompetence of internal os (IIOC) was higher in Group 3 (30.6%) compared with that in Group 1 (14.4%) ($P=0.001$) (OR 2.58; 95% CI 1.46–4.57) and in Group 2 (20.3%) ($P=0.024$) (OR 2.61; 95% CI 1.14–5.97). Rate of late preterm delivery was higher in Group 3 (69.4%) compared with that in Group 1 (39.2%) ($P=0.001$) (OR 3.78; 95% CI 2.34–6.09) but no difference compared with

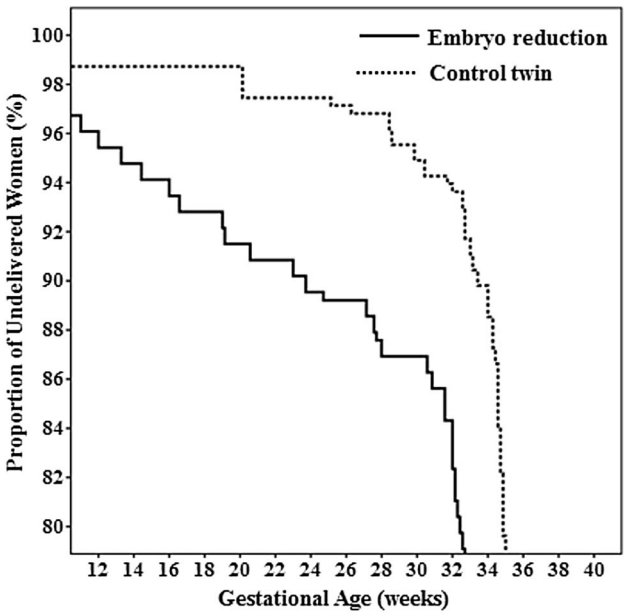

Fig. 2 Survival curves of twin pregnancies that remained undelivered across gestation with embryo reduction

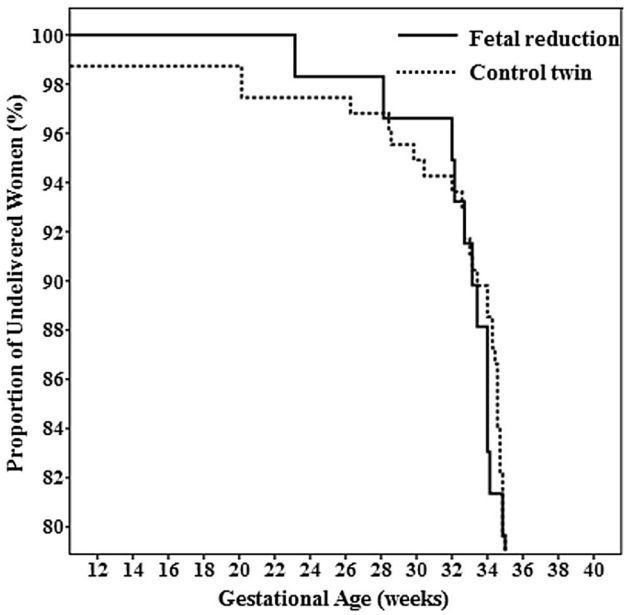

Fig. 3 Survival curves of twin pregnancies that remained undelivered across gestation with fetal reduction

that in Group 2. The groups did not differ with respect to the mean birth weights, and NICU admission rate.

Discussion

To the best of our knowledge, this is the first study to compare both the outcome of ER or FR with the control group. After adjustment, the fetal loss rate, which was defined as the loss of one or two fetuses during pregnancy, was comparable between FR group (6.8%) and the control group (3.8%), whereas a higher fetal loss rate was observed in the ER group (14.4%). The loss rate in this study is in line with reported literature values, varying between approximately 3% and 8% [11–13]. In the same manner, miscarriage rate was comparable between FR group (1.7%) and the control group (1.3%), whereas a higher miscarriage rate was observed in the ER group (6.5%). The mean gestational age of delivery had no significant difference between the groups. Overall, pregnancy outcomes following FR were better than ER when comparing with the control group.

A fetal loss of 6.5–16% has been reported in literature after MPR, although this incidence depends not only on operator's experience but also on gestational age at reduction, number of fetuses reduced, and the patient factors [12, 14, 15]

Transvaginal ER is more acceptable from both religious and ethical perspectives because it is performed earlier than FR, and toxic substances are not necessary [16]. The higher rate of overall fetal loss in ER group is to be expected, owing to the timing of reduction. The possibility of spontaneous demise of one of the fetuses may occur after the ER procedure [17, 18]. Spontaneous fetal abortion rate is 12–30% in ART cycles and even as high as 50–80% in triplet or higher-order gestation, and occurs within 12 weeks in 50% of cases [19–21]. Two studies have described pregnancy outcome in ER in twin pregnancies and compared with non-reduced twins [22, 23]. Mansour et al. concluded that the spontaneous abortion rate, fetal loss rate, gestational age at delivery, and birth weight of twin pregnancies after ER were similar to non-reduced twins [22]. In a prospective cohort study of Hass et al., they concluded the ER in triplets to twins seems to be comparable to the outcome of non-reduced twins. However, the perinatal outcome of ER in above quadruplets to twins was not as favorable as ER in triplets for birth weight and preterm delivery rate. They mentioned the advantages of FR and suggested that bER is also safe, and for some patients ER is seen to be psychologically advantageous over FR [23]. On the contrary, in our study, the ER group had a higher fetal loss and miscarriage rate compared to the control group.

Comprehensive anomaly scans using ultrasound, chorionic villus sampling, and non-invasive prenatal screening can be done before FR, which may allow the selection of which fetus to reduce [24]. Several studies in literature

Table 2 Obstetrical outcomes

	Group 1, embryo reduction ($n=153$)	Group 2, fetal reduction ($n=59$)	Group 3, control twins ($n=157$)	Group 1 vs. 3 adjusted p value	Group 2 vs. 3 adjusted p value
Overall fetal loss[a]	22 (14.4%)	4 (6.8%)	6 (3.8%)	0.003 OR 0.24 (95% CI 0.09–0.60)	NS
All surviving	131 (85.6%)	55 (93.2%)	151 (96.2%)	0.003 OR 4.26 (95% CI 1.66–10.94)	NS
None surviving	14 (9.2%)	1 (1.7%)	5 (3.2%)	0.036 OR 0.33 (95% CI 0.12–0.93)	NS
Miscarriage 12–24 weeks	10 (6.5%)	1 (1.7%)	2 (1.3%)	0.047 OR 0.21 (95% CI 0.45–0.98)	NS
Early preterm delivery	22 (14.4%)	6 (10.2%)	12 (7.6%)	NS	NS
Late preterm delivery	60 (39.2%)	32 (54.2%)	109 (69.4%)	0.001 OR 3.78 (95% CI 2.34–6.09)	NS
Term delivery	57 (37.3%)	20 (33.9%)	32 (20.4%)	0.001 OR 0.42 (95% CI:0.25–0.70)	NS
Gestational diabetes	10 (6.5%)	5 (8.5%)	22 (14.0%)	0.034 OR 2.33 (95% CI 1.06–5.10)	NS
Hypertensive disorders	9 (5.9%)	6 (10.2%)	17 (10.8%)	NS	NS
PPROM	23 (15.0%)	7 (11.1%)	10 (6.4%)	0.012 OR 0.37 (95% CI 0.17–0.80)	NS
IIOC	22 (14.4%)	12 (20.3%)	48 (30.6%)	0.001 OR 2.58 (95% CI 1.46–4.57)	0.024 OR 2.61 (95% CI 1.14–5.97)
Gestational age at delivery	34.1 ± 6.4	35.7 ± 2.5	35.2 ± 4.0	NS	NS
Birth weight (g)	2345 ± 441	2370 ± 388	2377 ± 352	NS	NS
NICU admission rate	50 (38.2%)	23 (42.6%)	74 (48.4%)	NS	NS

Data are represented as mean value ±SD or *n* (%)

PPROM preterm premature rupture of membranes, *IIOC* incompetent of internal os of cervix, *NS* not significant, *NICU* neonatal intensive care unit

[a]Overall fetal loss, defined as the loss of one or two fetuses during pregnancy

Table 3 Reported outcomes of embryo reduction (ER) in twin and control twin (CT) pregnancies

	Year published	Number (ER vs. CT)	Miscarriage (12–24 weeks) (ER vs. CT)	Total fetal loss rate (ER vs. CT)	Mean gestational age (ER vs. CT)
Mansour et al. [22]	1999	45 vs. 40	8.8% vs. 10%		36.9 vs. 36.5 weeks
Hass et al. [23][a]	2014	77 vs. 78	3.9% vs. 0%	6.5% vs. 5.1%	35.6 vs. 36.3 weeks
Present study	2018	153 vs. 157	6.5% vs. 1.3%	14.4% vs. 3.8%	34.1 vs. 35.2 weeks

[a]Prospective cohort study

that describe obstetric outcomes after reduction from HOMPs in twins between 11 and 14 weeks of gestation showed that FR was not associated with an increased risk of adverse pregnancy outcome compared to non-reduced dichorionic twins [25–29] (Table 3). Similarly, our study showed no difference in obstetrical outcomes in the non-reduced control group and FR group. The proportion of miscarriage rate throughout the published literature was heterogeneous, and this might be due to differently defined gestational age of miscarriage and some studies had a control group that included spontaneously conceived twins. However, most studies showed no statistical difference between the FR group and the control group in obstetrical outcomes. As mentioned above, ART twins had a greater risk of adverse perinatal outcome including preterm birth, low birth weight and death compared with spontaneously conceived twins [8, 9]. On the contrary, Cheang et al., showed that 353 cases of FR was associated with a higher incidence of extreme prematurity, prematurity, and low birth weight compared with the group of 389 cases of non-reduced twins and these findings were more pronounced among patients with a higher initial number of fetuses [25] (Table 4).

To our knowledge, a direct comparison of the obstetrical outcome between non-reduced twins with ER or SF twins has limited data in literature. The control group in our study had a higher rate of IIOC and this might be explained due to the fact that, our institution is a tertiary center hospital that includes a high-risk pregnancy center. A higher rate of IIOC may have contributed to a higher proportion of late preterm delivery compared to MPR groups**.** Also, the patients in MPR group had the tendency of getting more comprehensive prenatal care because of undergoing the invasive procedure in the first or second trimester.

Our study's limitations include its retrospective nature. The study's tertiary university hospital setting may have led to more adverse outcomes. This study's strengths are associated with it being a single center study with a relatively large sample size, and the adequate follow-up interval between the procedure and the delivery. The data were not influenced by performance variability, because FR was performed by a single physician, and ER was performed by two highly skilled physicians.

In conclusion, at the present time, we regard MPR as a clinically necessary procedure to prevent the complications of HOMPs. This study which included patients with similar obstetric care has clearly demonstrated that in comparing with non-reduced twin, FR compared to ER has advantages in reducing risk of spontaneous miscarriage, availability of nuchal translucency screening, and anatomy scan to rule out major anomalies before reduction. This information should be taken into account when counseling couples with HOMPs who considers MPR.

Table 4 Reported outcomes of fetal reduction (FR) in twin and control twin (CT) pregnancies

	Year published	Number (FR vs. CT)	Miscarriage (12–24 weeks) (FR vs. CT)	Total fetal loss rate (FR vs. CT)	Mean gestational age (FR vs. CT)
Lipitz et al. [29]	1996	43 vs. 134	2.3% vs. 0.7% (25–30 wks)		36.0 vs. 36.9 wks
Antasklis et al. [26]	1998	158 vs. 135	10.6% vs. 9.5% (28 wks)		35.7 vs. 35.1 wks
Selam et al. [28]	1999	77 vs. 140	5.2% vs. 2.9% (24–28 wks)		35.4 vs. 35.5 wks
Hwang et al. [27]	2002	54 vs. 406	3.9% vs. 4% (< 24 wks)	–	35.4 vs. 36 wks
Cheang et al. [25]	2007	353 vs. 389	4.5% vs. 1.8% (28 wks)*	1.4% vs. 2.3%	35.2 vs. 35.8 wks*
Present study	2018	59 vs. 157	1.7% vs. 1.3%	6.8% vs. 3.8%	35.7 vs. 35.2 wks

wks weeks

*Statistically significant ($P < 0.05$); total fetal loss, defined as one or two fetal losses throughout the pregnancy

Author contributions MSK: Manuscript writing, SK: Protocol/project development, data management, EDN: Manuscript writing/editing, JI: Data collection, EA: Data analysis, JES: Data collection, MJM: Protocol/project development.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. No Committee Opinion, 719 (2017) Multifetal pregnancy reduction. Obstet Gynecol 130(3):e158–e163. https://doi.org/10.1097/aog.0000000000002302
2. Garg P, Abdel-Latif ME, Bolisetty S, Bajuk B, Vincent T, Lui K (2010) Perinatal characteristics and outcome of preterm singleton, twin and triplet infants in NSW and the ACT, Australia (1994–2005). Arch Dis Child Fetal Neonatal Ed 95(1):F20–24. https://doi.org/10.1136/adc.2009.157701
3. Qin JB, Sheng XQ, Wang H, Chen GC, Yang J, Yu H, Yang TB (2017) Worldwide prevalence of adverse pregnancy outcomes associated with in vitro fertilization/intracytoplasmic sperm injection among multiple births: a systematic review and meta-analysis based on cohort studies. Arch Gynecol Obstet 295(3):577–597. https://doi.org/10.1007/s00404-017-4291-2
4. Zipori Y, Haas J, Berger H, Barzilay E (2017) Multifetal pregnancy reduction of triplets to twins compared with non-reduced triplets: a meta-analysis. Reprod Biomed Online 35(3):296–304. https://doi.org/10.1016/j.rbmo.2017.05.012
5. Kim MS, Choi DH, Kwon H, Ahn E, Cho HY, Baek MJ, Shin JE, Moon MJ (2018) Procedural and obstetrical outcomes after embryo reduction or fetal reduction in multifetal pregnancies: a retrospective study. Ultrasound Obstet Gynecol. https://doi.org/10.1002/uog.19024
6. Dodd J, Crowther C (2004) Multifetal pregnancy reduction of triplet and higher-order multiple pregnancies to twins. Fertil Steril 81(5):1420–1422. https://doi.org/10.1016/j.fertnstert.2003.11.028
7. Egbe TO, Sandjon G, Ourtchingh C, Simo A, Priso EB, Benifla JL (2016) In-vitro fertilization and spontaneous pregnancies: matching outcomes in Douala Cameroon. Fertil Res Pract 2:1. https://doi.org/10.1186/s40738-015-0013-2
8. Chung K, Coutifaris C, Chalian R, Lin K, Ratcliffe SJ, Castelbaum AJ, Freedman MF, Barnhart KT (2006) Factors influencing adverse perinatal outcomes in pregnancies achieved through use of in vitro fertilization. Fertil Steril 86(6):1634–1641. https://doi.org/10.1016/j.fertnstert.2006.04.038
9. Hansen M, Colvin L, Petterson B, Kurinczuk JJ, de Klerk N, Bower C (2009) Twins born following assisted reproductive technology: perinatal outcome and admission to hospital. Hum Reprod 24(9):2321–2331. https://doi.org/10.1093/humrep/dep173
10. Salomon LJ, Alfirevic Z, Bilardo CM, Chalouhi GE, Ghi T, Kagan KO, Lau TK, Papageorghiou AT, Raine-Fenning NJ, Stirnemann J, Suresh S, Tabor A, Timor-Tritsch IE, Toi A, Yeo G (2013) ISUOG practice guidelines: performance of first-trimester fetal ultrasound scan. Ultrasound Obstet Gynecol 41(1):102–113. https://doi.org/10.1002/uog.12342
11. Evans MI, Berkowitz RL, Wapner RJ, Carpenter RJ, Goldberg JD, Ayoub MA, Horenstein J, Dommergues M, Brambati B, Nicolaides KH, Holzgreve W, Timor-Tritsch IE (2001) Improvement in outcomes of multifetal pregnancy reduction with increased experience. Am J Obstet Gynecol 184(2):97–103. https://doi.org/10.1067/mob.2001.108074
12. Stone J, Ferrara L, Kamrath J, Getrajdman J, Berkowitz R, Moshier E, Eddleman K (2008) Contemporary outcomes with the latest 1000 cases of multifetal pregnancy reduction (MPR). Am J Obstet Gynecol 199 (4):406 e401–404. https://doi.org/10.1016/j.ajog.2008.06.017
13. Hershko-Klement A, Lipitz S, Wiser A, Berkovitz A (2013) Reduced versus nonreduced twin pregnancies: obstetric performance in a cohort of interventional conceptions. Fertil Steril 99(1):163–167. https://doi.org/10.1016/j.fertnstert.2012.09.005
14. Evans MI, Ciorica D, Britt DW, Fletcher JC (2005) Update on selective reduction. Prenat Diagn 25(9):807–813. https://doi.org/10.1002/pd.1261
15. Timor-Tritsch IE, Bashiri A, Monteagudo A, Rebarber A, Arslan AA (2004) Two hundred ninety consecutive cases of multifetal pregnancy reduction: comparison of the transabdominal versus the transvaginal approach. Am J Obstet Gynecol 191(6):2085–2089. https://doi.org/10.1016/j.ajog.2004.05.024
16. Coffler MS, Kol S, Drugan A, Itskovitz-Eldor J (1999) Early transvaginal embryo aspiration: a safer method for selective reduction in high order multiple gestations. Hum Reprod 14(7):1875–1878
17. Haas J, Barzilay E, Hourvitz A, Dor J, Lipitz S, Yinon Y, Shlomi M, Shulman A (2016) Outcome of early versus late multifetal pregnancy reduction. Reprod Biomed Online 33(5):629–634. https://doi.org/10.1016/j.rbmo.2016.08.015
18. Sun L, Jiang LX, Chen HZ (2017) Obstetric outcome of vanishing twins syndrome: a systematic review and meta-analysis. Arch Gynecol Obstet 295(3):559–567. https://doi.org/10.1007/s00404-017-4289-9
19. Bhandari S, Ganguly I, Agrawal P, Bhandari S, Singh A, Gupta N (2016) Comparative analysis of perinatal outcome of spontaneous pregnancy reduction and multifetal pregnancy reduction in triplet pregnancies conceived after assisted reproductive technique. J Hum Reprod Sci 9(3):173–178. https://doi.org/10.4103/0974-1208.192058
20. Dickey RP, Taylor SN, Lu PY, Sartor BM, Storment JM, Rye PH, Pelletier WD, Zender JL, Matulich EM (2002) Spontaneous reduction of multiple pregnancy: incidence and effect on outcome. Am J Obstet Gynecol 186(1):77–83
21. Zhang YL, Wang XY, Wang F, Su YC, Sun YP (2015) Clinical analysis of spontaneous pregnancy reduction in the patients with multiple pregnancies undergoing in vitro fertilization/intracytoplasmic sperm injection-embryo transfer. Int J Clin Exp Med 8(3):4575–4580
22. Mansour RT, Aboulghar MA, Serour GI, Sattar MA, Kamal A, Amin YM (1999) Multifetal pregnancy reduction: modification of the technique and analysis of the outcome. Fertil Steril 71(2):380–384
23. Haas J, Hourvitz A, Dor J, Elizur S, Yinon Y, Barzilay E, Shulman A (2014) Perinatal outcome of twin pregnancies after early transvaginal multifetal pregnancy reduction. Fertil Steril 101(5):1344–1348. https://doi.org/10.1016/j.fertnstert.2014.01.032
24. Stone J, Belogolovkin V, Matho A, Berkowitz RL, Moshier E, Eddleman K (2007) Evolving trends in 2000 cases of multifetal pregnancy reduction: a single-center experience. Am J Obstet Gynecol 197 (4):394 e391–394. https://doi.org/10.1016/j.ajog.2007.06.056
25. Cheang CU, Huang LS, Lee TH, Liu CH, Shih YT, Lee MS (2007) A comparison of the outcomes between twin and reduced twin pregnancies produced through assisted reproduction. Fertil Steril 88(1):47–52. https://doi.org/10.1016/j.fertnstert.2006.11.084
26. Antsaklis AJ, Drakakis P, Vlazakis GP, Michalas S (1999) Reduction of multifetal pregnancies to twins does not increase obstetric or perinatal risks. Hum Reprod 14(5):1338–1340

27. Hwang JL, Pan HS, Huang LW, Lee CY, Tsai YL (2002) Comparison of the outcomes of primary twin pregnancies and twin pregnancies following fetal reduction. Arch Gynecol Obstet 267(2):60–63. https://doi.org/10.1007/s00404-001-0279-y
28. Selam B, Lembet A, Stone J, Lapinski R, Berkowitz RL (1999) Pregnancy complications and neonatal outcomes in multifetal pregnancies reduced to twins compared with nonreduced twin pregnancies. Am J Perinatol 16(2):65–71. https://doi.org/10.1055/s-2007-993838
29. Lipitz S, Uval J, Achiron R, Schiff E, Lusky A, Reichman B (1996) Outcome of twin pregnancies reduced from triplets compared with nonreduced twin gestations. Obstet Gynecol 87(4):511–514. https://doi.org/10.1016/0029-7844(95)00469-6