BMC Pregnancy and Childbirth

RESEARCH

Open Access

Pregnancy and obstetric outcomes of dichorionic and trichorionic triamniotic triplet pregnancy with multifetal pregnancy reduction: a retrospective analysis study

Shuhua Liu[1,2], Guanjian Li[1,3,4,5], Chao Wang[1,3,4,5], Ping Zhou[1,3,4,5], Zhaolian Wei[1,3,4,5*] and Bing Song[1,3,4,5*]

Abstract

Background: It is generally beneficial for triplet gestation or high-order multiple pregnancies to operate multifetal pregnancy reduction (MFPR) after assisted reproductive techniques. However, data on pregnancy outcomes is lacking regarding dichorionic triamniotic (DCTA) and trichorionic triplets (TCTA) pregnancy.

Method: This research analyzes the difference between 128 DCTA and 179 TCTA pregnancies with or without MFPR after in vitro fertilization/intracytoplasmic sperm injection cycles between January 2015 and June 2020. The subdivided subgroups of the two groups are reduction to singleton, reduction to dichorionic twins, and expectant management groups. We also compare the pregnancy and obstetric outcomes between 2104 dichorionic twins and 122 monochorionic twins.

Result: The research subgroups were DCTA to monochorionic singleton pregnancies ($n=76$), DCTA to dichorionic twin pregnancies ($n=18$), DCTA-expectant management ($n=34$), TCTA to monochorionic singleton pregnancies ($n=31$), TCTA to dichorionic twin pregnancies ($n=130$), and TCTA-expectant management ($n=18$). In DCTA-expectant management group, the complete miscarriage rate is dramatically higher, and the survival rate and the rate of take-home babies are lower. However, there was no difference between the rates of complete miscarriages, survival rates, and take-home babies in TCTA-expectant management group. But the complete miscarriage rate of DCTA-expectant management was obviously higher than that of TCTA-expectant management group (29.41 vs. 5.56%, $p=0.044$). For obstetric outcomes, MFPR to singleton group had higher gestational week and average birth weight, but lower premature delivery, gestational hypertension rates and low birth weight in both DCTA and TCTA pregnancy groups (all $p<0.05$). DCTA to monochorionic singleton had the lowest incidence of gestational diabetes, whereas The subdivided subgroups of TCTA had no significant difference in the incidence of gestational diabetes. Monochorionic twins have higher rates of complete, early, and late miscarriage, premature delivery, and late premature delivery, and lower survival rate ($p<0.05$).

Conclusion: MFPR could improve gestational week and average birth weight, reducing premature delivery, LBW, and gestational hypertension rates in DCTA and TCTA pregnancies. Monochorionic twins have worse pregnancy and

*Correspondence: weizhaolian_1@126.com; songbing060907@126.com
[5] Anhui Province Key Laboratory of Reproductive Health and Genetics, Hefei 230032, China
Full list of author information is available at the end of the article

obstetric outcomes. MFPR to singleton is preferable recommended in the pregnancy and obstetric management of complex triplets with monochorionic pair.

Keywords: Multifetal pregnancy reduction, Obstetric outcomes, Dichorionic triamniotic, Assisted reproductive technology

Introduction

Over the past decades, the incidence of multiple pregnancies has obviously increased [1], mainly owing to the wide application of assisted reproductive techniques (ART) [2]. Controlled ovarian hyperstimulation is involved in ART for the initial step, which is used to obtain multiple embryos [3], and multiple embryo transplants are used to maximize pregnancy rates in ART [4, 5]. Our previous study showed that the young mother's age, high-quality embryos are risk factors of monochorionic-diamniotic (MC-DA) twin in assisted reproduction [6]. With the increase in the number of embryos, the incidence of fetal and maternal complications is also elevated. These risks include gestational diabetes mellitus, gestational hypertension and medical and surgical conditions aggravation. Meanwhile, there are higher risks of miscarriage, embryonic growth restriction, premature delivery, and the complications of fetal respiratory diseases and cerebral palsy caused by premature delivery [7, 8] . In addition, a monochorionic pregnancy is associated with specific complications caused by vascular anastomoses in the common placenta, which impact infant and maternal morbidity and mortality [9]. Monochorionic twins have attracted extensive attention as a result of the associated complications, for example twin anemia-polycythemia sequence (TAPS), twin-to-twin transfusion syndrome (TTTS), and selective intrauterine growth restriction (SIGR).

Multifetal pregnancy reduction (MFPR) is extensively used to decrease maternal and fetal risks to raise the likelihood of good pregnancy outcomes [10, 11], but no agreed optimal strategy exists. Some scholars think that reduction to single can achieve the most perfect pregnancy and obstetric outcomes [12, 13], however other studies have found that the rate of miscarriage could be increased after early MFPR [14, 15]. In addition, there are few published reports concerning the expectant management of DCTA pregnancies, in which a pair of monochorionic diamniotic twins use a placenta at the same time.

This study aimed to analyze the differences between MFPR and expectant management in DCTA and TCTA pregnancies, and analyze the differences between monochorionic and dichorionic twins' pregnancies.

Materials and methods

We retrospectively analyzed 128 DCTA cases, 179 TCTA cases, 2104 dichorionic twin cases, and 122 monochorionic twin cases from January 2015 to June 2020 at the Reproductive Medicine Center, Department of Obstetrics and Gynecology, the First Affiliated Hospital of Anhui Medical University. The subdivided subgroups of the two groups are DCTA reduction to monochorionic singleton ($n=76$), DCTA reduction to dichorionic-diamniotic (DCDA) twin ($n=18$) and DCTA-expectant management ($n=34$) groups, and TCTA reduction to monochorionic singleton ($n=31$), TCTA reduction to dichorionic twin ($n=130$), and TCTA-expectant management ($n=18$) groups.

All of MFPRs were performed 6–8 weeks after embryo transplant (ET). Experienced doctors in our Reproductive Medicine Center carried out these operations, which involve the puncture and aspiration of selected embryonic parts without administering any medications, under transvaginal ultrasound guidance. Pregnancies were diagnosed by transvaginal ultrasound to determine the number of fetal and monochorionic or dichorionic pregnancies according to the ultrasound presence of the "T sign" or "lambda sign". Couples were informed about the disadvantages of triplet or high-order multiple pregnancies. We finally decided to perform the operation based on the couples' intention, the situation, and the fetus's condition. Pregnant mothers had been protected from infection by administering antibiotics for 1 week preoperatively, and the fetuses were inspected in utero on the 1st and 5th day postoperatively.

Statistical analysis

Statistical analysis were performed using the SPSS 22.0 software package (SPSS Inc., Chicago, IL). Because the data were normally distributed, continuous variables are expressed as mean ± standard deviation (SD). Between-group differences were evaluated using a t-test, and the fisher's exact test or the chi-squared test were used to analyze the difference between percentages. The threshold of the data discrepancies was set at $P<0.05$.

Results

The maternal demographics and clinical characteristics in TCTA and DCTA pregnancies

The clinical features of DCTA and TCTA groups included in this study are listed in Table 1 and Table 2. There were no statistically significant differences of

the maternal age between the subgroups. Body mass index (BMI), the interval between transplantation and MFPR, duration and type of infertility, frozen embryo transplant (FET), and insemination methods were also matched in both groups with no significant differences($P > 0.05$).

Pregnancy and obstetric outcomes in DCTA and TCTA pregnancies

DCTA reduction to singleton group had lower rates of complete miscarriage, early miscarriage, higher rates of survival and take-home babies than DCTA- expectant management group (Table 3). Furthermore, the obstetric outcomes were better in DCTA reduction to singleton pregnancy group than DCTA reduction to twin and DCTA-expectant management groups, which shows that

Table 1 Maternal demographics and clinical characteristics in DCTA pregnancy

	DCTA reduction to twin ($n=18$)	DCTA reduction to singleton ($n=76$)	DCTA-expectant management ($n=34$)	*P* value
Clinical characteristic				
Maternal age (years)	30.33 ± 4.37	29.47 ± 4.07	29.21 ± 4.35	0.645
Interval between transplantation and MFPR (days)	41.83 ± 6.38	40.08 ± 6.19		0.285
BMI (kg/m^2)	21.09 ± 2.70	22.39 ± 2.93	21.05 ± 2.10	0.069
Duration of infertility (years)	3.53 ± 2.05	3.46 ± 2.56	3.41 ± 2.16	0.986
Infertility type				
Primary, n (%)	(14/18) 77.78	(42/76) 55.26	(17/34) 50.00	
Secondary, n (%)	4	34	17	0.139
FET (N)				
not-used (%)	(7/18) 38.89	(26/76) 34.21	(9/34) 26.47	
used (%)	11	50	25	0.610
Insemination methods				
ICSI, n (%)	(7/18) 61.70	(29/76) 63.64	(11/34) 47.83	
IVF, n (%)	11	47	23	0.826

No significant difference was found between the three sets of data in the DCTA group

Table 2 Comparison of the maternal demographics and clinical characteristics in TCTA pregnancies

	TCTA reduction to single ($n=31$)	TCTA reduction to twin ($n=130$)	TCTA-expectant management ($n=18$)	*P* value
Clinical characteristic				
Maternal age (years)	32.57 ± 3.77	32.20 ± 4.57	32.00 ± 3.48	0.634
Interval between transplantation and MFPR (days)	38.86 ± 3.34	37.52 ± 5.19		0.707
BMI (kg/m^2)	21.41 ± 1.89	22.31 ± 2.92	22.14 ± 3.16	0.235
Duration of infertility (years)	3.94 ± 1.67	4.06 ± 2.51	5.11 ± 3.09	0.073
Infertility type				
Primary, n (%)	(19/31)61.29	(79/130)60.77	(9/18)50.00	
Secondary, n (%)	12	51	9	0.671
FET (N)				
not-used (%)	(7/31)22.58	(26/130)20.00	(6/18)33.33	
Used (%)	24	104	12	0.435
Insemination methods				
ICSI, n (%)	(7/31) 22.58	(35/130) 26.92	(3/18) 16.67	
IVF, n (%)	24	95	15	0.602

No significant difference was found between the three sets of data in the TCTA group

Table 3 Pregnancy and obstetric outcomes in DCTA pregnancy

	DCTA reduction to twin (*n* = 18)	DCTA reduction to singleton (*n* = 76)	DCTA-expectant management (*n* = 34)	*P* value
pregnancy outcomes				
gestational week (weeks)	37.19 ± 2.90[a]	38.85 ± 1.69[a,b]	35.33 ± 2.35	**p < 0.001**
Average birth weight (g)	2734.09 ± 615.55[a]	3276.49 ± 515.64[a,b]	2232.65 ± 603.53	**p < 0.001**
Complete miscarriage rate (%)	(2/18) 11.11	(2/76) 2.63[a]	(10/34) 29.41	**P < 0.001**
Early miscarriage rate(< 12 weeks) (%)	(1/18) 5.55	(0/76) 0.00[a,b]	(5/34) 14.71	**p = 0.003**
Late miscarriage rate (12–28 weeks)	(1/18) 5.55	(2/76) 2.63[a]	(5/34) 14.71	**p = 0.042**
Premature delivery rate (%)	(7/16)43.75	(7/74) 9.46[a,b]	(16/24) 66.67	**p < 0.001**
Early premature delivery (28–34 weeks) (%)	(1/16) 6.25	(3/74) 4.05[a]	(5/16) 31.25	**p = 0.006**
Late premature delivery (34-37 weeks) (%)	(6/16)37.5	(4/74) 5.41[a,b]	(11/16) 68.75	**p < 0.001**
survival rate(%)	(16/18)88.89	(74/76) 97.37[a]	(24/34) 70.59	**p < 0.001**
One survivor	10	74	6	/
Two survivors	6	–	11	/
Three survivors	–	–	7	/
Take baby home rate (%)	(16/18) 88.89	(74/76) 97.37[a]	(24/34) 70.59	**p < 0.001**
Cesarean section rate (%)	(13/16) 81.25	(60/74) 81.08	(23/24) 95.83	*p* = 0.220
LBW < 2500 g (%)	(9/22) 40.91	(3/74) 4.05[a,b]	(24/49) 48.98	**p < 0.001**
VLBW < 1500 g (%)	(1/22) 4.55	(1/74) 1.35	(3/49) 6.12	*p* = 0.358
Percentage of boys (%)	(10/12) 83.33	(42/74) 56.76	(26/49) 6.12	*p* = 0.161
obstetric outcomes				
Gestational hypertension (%)	(2/16) 12.5	(3/74) 4.05[a]	(6/24) 25	**p = 0.007**
Gestational diabetes mellitus (%)	(3/16) 18.75	(1/74) 1.35[a,b]	(4/24) 16.67	**p = 0.004**

[a] Significant difference compared with the expectant management group

[b] Significant difference compared with the DCTA to twin group

DCTA reduction to singleton group had the longest gestational week and the highest average birth weight, while the rates of early miscarriage, premature delivery, late premature delivery, gestational diabetes mellitus, and LBW were the lowest. In addition, the rate of late miscarriage, early premature delivery, survival rate, gestational hypertension were all lower in DCTA to singleton group than in DCTA expectant management group. However, cesarean section rate, the rate of VLBW, and the percentage of boys were not significant different between three DCTA subgroups.

The premature delivery rate was highest in TCTA-expectant management group, but gestational week and average birth weight were lowest. However, complete miscarriage, survival rate, cesarean section, VLBW, and take-home baby rates or the percentage of boys were no significant difference between three TCTA subgroups (Table 4). The obstetric outcomes were similar in DCTA and TCTA pregnancies, and the MFPR to singleton group had the longest gestational week, highest average birth weight, and lowest rate of LBW. Conversely, the premature delivery and LBW rates were highest in DCTA-expectant management and TCTA-expectant management groups.

Comparison of pregnancy and obstetric outcomes in monochorionic and dichorionic twin pregnancies

We analyzed 2226 cases of twin pregnancies, including 122 cases of monochorionic and 2104 cases of dichorionic twins. The pregnancy and obstetric outcomes of the two groups were shown in Table 5. The results showed that monochorionic twin have higher rates of complete miscarriage (24.59 vs. 7.27%, $p < 0.001$), early miscarriage (13.93 vs. 2.04%, $p < 0.001$), late miscarriage (10.66 vs. 5.23%, $p < 0.05$), premature delivery (60.87 vs. 48.23%, $p < 0.05$), late premature delivery (50.00 vs. 36.90%, $p < 0.05$), and TTTS (3.28 vs. 0%, $p < 0.001$), but lower rates of survival rate (75.41 vs. 92.16%, $p < 0.001$), and multiple survival rates (61.48 vs. 78.33%, $p < 0.001$) than dichorionic twins.

Discussion

Multiple pregnancies significantly increase the incidence of severe fetal and maternal complications. To avoid these risks, we advocate single pregnancy in order to achieve good obstetric outcomes. To ensure both pregnancy rates and obstetric outcomes, we recommend the number of transfer embryos should not exceed two cleavage embryos or one blastocyst in the first cycle. Still, multiple

Table 4 Pregnancy and obstetric outcomes in TCTA pregnancy

	TCTA reduction to twin (*n* = 130)	TCTA reduction to singleton (*n* = 31)	TCTA-expectant management(*n* = 18)	*P* value
pregnancy outcomes				
gestational week (weeks)	35.99 ± 2.33[a]	38.00 ± 2.64[a,b]	34.64 ± 2.79	**p < 0.001**
Average birth weight (g)	2567.66 ± 571.38[a]	3105.38 ± 691.46[a,b]	2285.43 ± 613.71	**p < 0.001**
Complete miscarriage rate (%)	(5/130) 3.85	(3/31) 9.68	(1/18) 5.56	*p* = 0.309
Early miscarriage rate(< 12 weeks) (%)	(1/130) 0.77	(2/31) 6.45	(1/18) 5.56	*p* = 0.063
Late miscarriage rate (12–28 weeks)	(4/130) 3.08	(1/31) 3.23	(0/18) 0.00	*p* = 1.000
Premature delivery rate	(60/125) 48.00[a]	(5/28) 17.86[a,b]	(15/17) 88.24	**p < 0.001**
Early premature delivery (28–34 weeks) (%)	(20/125) 16.00	(1/28) 3.57	(2/17) 11.76	*p* = 0.235
Late premature delivery (34–37 weeks) (%)	(40/125) 32.00[a]	(4/28) 14.29[a]	(13/17) 74.47	**p < 0.001**
survival rate(%)	(124/130) 95.38	(28/31) 90.32	(17/18) 94.44	*p* = 0.482
One survivor	16	28	2	/
Two survivors	108	–	5	/
Three survivors	–	–	10	/
Take baby home rate (%)	(124/130) 95.38	(28/31) 90.32	(17/18) 94.44	*p* = 0.482
Cesarean section rate	(112/125) 89.6	(23/28) 82.14	(15/17) 88.24	*p* = 0.482
LBW < 2500 g (%)	(92/232) 39.66	(3/28)10.71[a,b]	(23/42) 54.76	**P = 0.001**
VLBW < 1500 g (%)	(28/232) 12.07	(1/28) 3.57[a]	(6/42) 14.29	**p = 0.359**
Percentage of boys (%)	(118/232)50.86	(14/28)50	(26/49)53.06	*P* = 0.432
obstetric outcomes				
Gestational hypertension (%)	(9/125)0.072	(0/28) 0[a]	(4/17)23.53	**P = 0.020**
gestational diabetes mellitus (%)	(5/125) 4	(1/28)3.57	(3/17)17.65	*P* = 0.087

[a] Significant difference compared with the expectant management group

[b] Significant difference compared with the TCTA to twin group

pregnancies are inevitable. There are many reasons for multiple pregnancy, such as maternal age, embryo quality, blastocyst transfer, laboratory environment, culture medium conditions, genes and genetic factors, zona pellucida operation, etc. Our previous study has confirmed that gestational age < 35 years old and blastocyst transfer are independent risk factors for monozygotic twinning (MZT) [6].

Multiple pregnancy can easily lead to gestational hypertension, gestational diabetes mellitus, intrahepatic cholestasis of pregnancy, anemia, premature rupture of membranes and premature delivery, low birth weight, and abnormal fetal development. Fetal reductions have emerged as a remedy to reduce the risks associated with multiple pregnancies. It is difficult to decide whether MFPR or not while considering the risk of abortion. The aim of this research was to compare the pregnancy and obstetric outcomes of different reduction tactics and expectant management in DCTA and TCTA pregnancies.

DCTA pregnancies have many associated risks, such as premature delivery, selective growth restriction, and fetal malformations. Monochorionic twins are associated with single placental bed vascular anastomoses, such as TTTS and selective intrauterine growth restriction [16, 17]. These adverse pregnancy and obstetric outcomes have led to search for a favorable fetal reduction strategy for reducing the occurrence of the aforementioned adverse events. However, although MFPR can reduce the premature delivery rate, the miscarriage rate may increase correspondingly. Therefore, no consensus exists on whether MFPR should be performed and the optimal number of fetal reductions in DCTA pregnancies [18]. Some research has shown that MFPR to singleton in DCTA may improve the pregnancy outcomes and positively alter gestational week, related to infant mortality and disability [9, 18–21].

A systematic review of different treatment strategies in DCTA suggested that expectant management is a reasonable option When survival rates are prioritized. Conversely, if minimizing the rate of severe premature delivery is the top priority, the best desirable choice is to reduce the number of fetuses [20]. The research of Chaveeva et al. supports the conclusion that embryo reduction increases the miscarriage rate but reduces the premature delivery rate in DCTA pregnancy [21]. Likewise, a smaller meta-analysis noted that the miscarriage rate of expectant management group were almost twice as likely as the MFPR group (8.1% vs. 4.4%) [22].

Table 5 Monochorionic and dichorionic twin pregnancies comparison

	Dichorionic twins ($n=2104$)	Monochorionic twins ($n=122$)	*P* value
Clinical characteristic			
Maternal age (years)	29.49 ± 3.69	29.58 ± 4.17	0.797
gestational week (weeks)	36.20 ± 2.27	36.05 ± 2.30	0.542
Average birth weight (g)	2612.53 ± 523.61	2566.37 ± 507.27	0.263
Proportion of primary infertility (%)	(1250/2104)59.41	(73/122)59.84	0.926
Fresh cycle ratio (%)	(632/2104)30.04	(34/122)27.87	0.611
pregnancy outcomes			
Complete miscarriage rate (%)	(153/2104)7.27	(30/122)24.59	**$p<0.001$**
Early miscarriage rate(< 12 weeks) (%)	(43/2104)2.04	(17/122)13.93	**$P<0.001$**
Late miscarriage rate (12–28 weeks)	(110/2104)5.23	(13/122)10.66	**0.011**
Premature delivery rate (%)	(941/1951)48.23	(56/92)60.87	**0.018**
Early premature delivery (28–34 weeks) (%)	(221/1951)11.33	(10/92)10.87	0.892
Late premature delivery (34-37 weeks) (%)	(720/1951)36.90	(46/92)50.00	**0.011**
survival rate rate (%)	(1939/2104)92.16	(92/122)75.41	**$p<0.001$**
Singleton survival rate rate (%)	(291/2104)13.83	(14/122)11.48	0.462
Twin survival rate rate (%)	(1648/2104)78.33	(75/122)61.48	$p<0.001$
Percentage of twins, one live, one stillbirth (%)	(0/2104)0	(3/122)2.46	$p<0.001$
Double stillbirth (%)	(12/2104)0.57	(0/122)0.00	1.000
Cesarean section rate (%)	(1776/1951)91.03	(86/92)93.48	0.419
LBW rate (%) (< 2500 g)	(1293/3611)35.81	(69/170)40.59	0.204
VLBW rate (< 1500 g) (%)	(100/3611)2.77	(3/170)1.76	0.628
Birth weight discordance>25% (%)	(119/3320)3.58	(5/78)6.41	0.207
Percentage of boys (%)	(1997/3611)55.30	(100/170)58.82	0.367
obstetric outcomes			
Gestational hypertension (%)	(105/2104)4.99	(8/122)6.56	0.443
gestational diabetes mellitus (%)	(48/2104)2.28	(5/122)4.10	0.210
intrahepatic cholestasis of pregnancy (%)	(8/2104)0.38	(2/122)1.64	0.101
twin-twin transfusion syndrome (%)	(0/2104)0	(4/122)3.28	**$p<0.001$**
Neonatal deformities (%)	(24/3611)0.66	(1/170)0.59	1.000

However, another small meta-analysis found no difference in the miscarriage rate at 24 weeks between multiple reduction group and expectant management group [23]. A larger meta-analysis by Zipori Y et al. found that reduction of triplet pregnancy to twins' group had a lower rate of preterm birth before 32 or 28 weeks of gestation and maternal complications, such as gestational diabetes, gestational hypertensive disorders, need for antenatal hospitalization, and cesarean delivery rates and a higher rate of fetal birth weight compared with the expectant management group, and the miscarriage rate did not increase within 24 weeks of gestation. However, the rates of small for gestational age (SGA) births, overall survival are comparable between reduction group and expectant management group [24]. Our research found that the complete miscarriage rate was significantly reduced from 29.41 to 2.63% in DCTA reduction to singleton than DCTA-expectant management group. However, no difference was found in complete miscarriage rates between the TCTA reduction group and expectant management group. And in this study, the complete miscarriage rate after reduction was lower than previous addressed. This finding demonstrates that DCTA reduction to singleton is safe, and the miscarriage rate has not increased during the 6–8 weeks gestational period.

The timing of fetal reduction in multiple pregnancies has previously been studied in detail. The miscarriage rate after reduction in multiple pregnancies also varies at different times. A study by Evans showed that pregnancy loss rates were 5.4, 8.7, 6.8 and 9.1% when the timing of fetal reduction was 9–12 weeks, 13–18 weeks,19–24 weeks, and ≥ 25 weeks, respectively, but the data were not statistically different [25]. Another study showed that the miscarriage rates were 4.3 and 4.0% when MFPR to twin at 11–12 weeks and 13–14 weeks, respectively. The data are also not significantly different

[26]. Haas et al. suggested that compared MFPR to twin with MFPR to singleton at 6–8 weeks gestation, the miscarriage rates before 24 weeks were 3.6 and 5.3%, respectively [14]. MFPR at 11–14^{+6} weeks had a lower rate of spontaneous abortion compared with 15–24^{+6} weeks' gestation (6.5% vs. 14.9%, respectively) [27]. In this study, DCTA reduction to singleton achieved a lower miscarriage rate of 2.63% at 6–8 weeks' gestation compared to DCTA-expectant management group.

DCTA reduction to twin group are composed of 18 underwent selective reduction of one fetuses of the monochorionic-diamniotic twin. Because of the vascular anastomosis between monochorionic twins [28]. when reducing one of the monochorionic twins, more caution should be undertaken while performing fetal reduction surgery, and the complete miscarriage rate of TCTA-expectant management was significantly lower than that of DCTA-expectant management in our study.

There were significant differences between the subgroups of participants who underwent MFPR to singleton compared to those who choose MFPR to twin or expectant management in DCTA and TCTA pregnancies, which shows that MFPR reduction to singleton improved pregnancy and obstetric outcomes by obviously reducing the risks of premature delivery and LBW, and obviously raising gestational week and average birth weight in DCTA and TCTA pregnancies. DCTA and TCTA reduction to singleton group had the lowest rate of preterm birth. In terms of obstetric complications, the DCTA reduction to singleton group had the lowest incidence of gestational diabetes. Similarly, other findings also showed that the triplet pregnancy to twins group had a lower incidence of gestational diabetes and preterm birth than the expectant management group [29]. Some researchers believe that the cause of preterm birth may be related to the relative lack of adequate uterine cavity and blood supply. Whereas the subdivided subgroups of TCTA had no significant difference in the incidence of gestational diabetes. This result may be related to the limited amount of data in the TCTA subgroup, and later studies can increase the amount of relevant data for further research. Thus, we didn't advocate expectant management for DCTA pregnancy.

Potassium chloride injection is not recommended for monochorionic pregnancy because the remaining fetus can be embolized by the drug through vascular anastomosis in the common placenta [30]. However, the laser technique of intrafetal interstitia to remove one monochorionic twin can also imperil the remaining twin [31]. Chaveeva et al. reported 61 pregnant women with DCTA whose pregancies were reduced to dichorionic twin pregnancy by intrafetal laser ablation; although 3% of cases of miscarriage occurred after reduction, nearly half of the cases occurred within 2 weeks after reduction [15]. Other studies show that the mechanical method of intracardiac puncture and aspiration is an effective and feasible MFPR method for reducing adverse pregnancy outcomes, including those in monochorionic twin pregnancies [32–35]. Therefore, we adopted the mechanical method of intracardiac puncture and aspiration to reduce the fetus during the 6–8 weeks gestational period.

The miscarriage rate of DCTA-expectant management group was obviously higher than DCTA reduction to singleton group, although the mechanism of miscarriage is not clear. Some researchers think the relative lack of adequate uterine cavity and blood provision is related to spontaneous fetal reduction in multifetal pregnancy [36]. However, we also found that pregnancy loss occurs after embryo reduction in DCTA and TCTA pregnancies. Compared TCTA reduction to twin with DCTA reduction to twin group, TCTA reduction to twin group would obtain the proportion of two babies is significantly higher than that of DCTA reduction to twin group. This dramatically higher singleton survival rate and dramatically lower twin survival rate in DCTA pregnancy is consistent with the findings of Li et al. [33]. According to some studies, the related mechanism of miscarriage caused by fetal reduction in DCTA may be considered as follows: firstly, injuries and infections caused by fetal reduction surgery in cases where miscarriage occurred within 2 weeks of fetal reduction. Secondly, the necrotic embryonic placental tissue causing the inflammation reaction is reabsorbed, which could cause miscarriage several weeks or months after fetal reduction [30, 37, 38] Therefore, when considering reducing the complications of pregnancy and adverse obstetric outcomes and choosing to reduce fetuses to dichorionic twins in DCTA pregnancies, couples should be informed about the higher risk of pregnancy loss. There was no significant difference in cesarean section rate and the percentage of boy between the three subgroups in DCTA and TCTA pregnancies. The main reason why there is no difference in the rate of cesarean section may be due to human factors rather than medical needs.

Due to the unique characteristics of monochorionic twin pregnancies in terms of the placental structure, some studies conclude that monochorionic twins have dramatically worse outcomes than dichorionic twins [31, 39, 40]. This may be attributable to the complications associated with monochorionic twins, including TTTS, TAPS, and SIGR, which are detrimental to maternal and fetal health. Liu et al.'s study shows that the pregnancy and obstetric outcomes of DCTA-monochorionic twin pregnancies are relatively worse than those retaining a single fetus but without statistical difference. It is concluded that compared with reducing one fetus in

monochorionic twins, reduction with a separate placenta might be an acceptable reduction strategy with a relatively lower miscarriage rate, despite the potential risks to monochorionic twins [19]. However, this research found that the complete miscarriage rate of the DCTA reduction to twin group is slightly higher than that of the DCTA reduction to singleton group, but there is no significant difference. Therefore, regarding the choice of DCTA to twin pregnancy, we must weigh the pros and cons and solicit the choice of couples, informing patients of the risks and benefits of reduction to one or two or expectant management.

This was a single-center retrospective comparative study, and some of the statistically insignificant results may be due to the limited number of patients in some subgroups. The Eligible patients are not randomly assigned to each group, so the results of the study may have some deviations. Due to different wishes and internal factors of the family, and ethical considerations, some couples may choose to undergo MFPR or not, and this research is unlikely to be suitable for randomized controlled trials. Some of the data were collected through telephonic interviews with women who had been pregnant many years before thereby the data could be prone to recall bias. Some of the strengths of our study include the relatively abundant reduction data, an extended research time frame, strict inclusion criteria, and detailed statistical methods. All reduction operations were performed by several highly skilled doctors in our center, thereby preventing significant differences in surgical results.

Conclusions

MFPR could improve pregnancy and obstetric outcomes for DCTA and TCTA pregnancies, and MFPR to single fetus could achieve a longer gestational week and higher average birth weight. It seems that dichorionic twins have better pregnancy outcomes than monochorionic twins. For DCTA pregnancy, it is highly recommended to reduce fetus to single for the best pregnancy and obstetric results. Fetal reduction is simply a remedy to reduce the risks related to multifetal pregnancy. With the rapid progress of embryo culture technology in vitro and high embryo implantation rate in China, single blastocyst transplant has been encouraged in more and more Reproductive Medicine Centers to prevent multifetal pregnancy.

Abbreviations

MFPR: Multifetal pregnancy reduction; DCTA: Dichorionic triamniotic triplet pregnancy; TCTA: Trichorionic triamniotic triplet pregnancy; ICSI: Intracytoplasmic sperm injection; IVF: In vitro fertilization; ART: Assisted reproductive technology; MC-DA: Monochorionic-diamniotic; DCDA: Dichorionic-diamniotic; TTTS: Twin-to-twin transfusion syndrome; SIGR: Selective intrauterine growth restriction; TAPS: Twin anemia-polycythemia sequence; ET: Embryo transplant; FET: Frozen embryo transplant; BMI: Body mass index; LBW: Low birth weight; VLBW: Very low birth weight; MZT: Monozygotic twinning; SGA: Small for gestational age.

Acknowledgments

We would like to thank all the patients who agreed to participate in this study.

Authors' contributions

SL and BS contributed to the conception and design. GL, CW and PZ contributed to the development of the methodology. BS and CW collected and analyzed the data. SL and BS contributed to the writing, review, and/or revision of the manuscript. PZ, BS and ZW contributed to administrative, technical, or material support. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due the containing information that could compromise research participant but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Review Board of The First Affiliated Hospital of Anhui Medical University (PJ20180707) and was conducted according to the Declaration of Helsinki principles. Written informed consents were obtained from all enrolled patients after an explanation of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Reproductive Medicine Center, Department of Obstetrics and Gynecology, the First Affiliated Hospital of Anhui Medical University, Hefei 230032, China. [2]Department of Obstetrics and Gynecology, Anhui Province Maternity and Child Health Hospital, Hefei 230000, China. [3]NHC Key Laboratory of Study on Abnormal Gametes and Reproductive Tract, Anhui Medical University, Hefei 230032, China. [4]Ministry of Education Key Laboratory of Population Health Across Life Cycle, Anhui Medical University, Hefei 230032, China. [5]Anhui Province Key Laboratory of Reproductive Health and Genetics, Hefei 230032, China.

Received: 28 August 2021 Accepted: 22 March 2022
Published online: 05 April 2022

References

1. American College of Obstetricians and Gynecologists 'Committee on Practice Bulletins—Obstetrics, Society for Maternal-Fetal Medicine. Multifetal Gestations: Twin, Triplet, and Higher-Order Multifetal Pregnancies: ACOG Practice Bulletin, Number 231. [J]. Obstet Gynecol. 2021;137:e145–62.
2. American College of Obstetricians and Gynecologists, Society for Maternal Fetal Medicine. ACOG practice bulletin no. 144: multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. Obstet Gynecol. 2014;123:1118–32.
3. Chaabane S, Sheehy O, Monnier P, Bissonnette F, Trasler JM, Fraser W, et al. Association between ovarian stimulators with or without intrauterine insemination, and assisted reproductive technologies on multiple births. Am J Obstet Gynecol. 2015;213:511.e1e511.e14.
4. Jan G. Single-embryo transfer versus multiple-embryo transfer. [J]. Reprod BioMed Online. 2009;null:63–70.

5. Azem F, Yaron Y, Amit A, Yovel I, Barak Y, Peyser MR, et al. Transfer of six or more embryos improves success rates in patients with repeated in vitro fertilization failures. Fertil Steril. 1995;63:1043–6.
6. Song B, Wei ZL, Xu XF, Wang X, He XJ, Wu H, et al. Prevalence and risk factors of monochorionic diamniotic twinning after assisted reproduction: a six-year experience base on a large cohort of pregnancies. PLoS One. 2017;12(11):e0186813.
7. Fajolu IB, Ezeaka VC, Adeniyi OF, Iroha EO, Egri-Okwaji MTC. Prevalence and outcome of higher order multiple pregnancies in Lagos. Nigeria J Matern Fetal Neonat Med. 2013;26:1342–5.
8. Pharoah POD. Risk of cerebral palsy in multiple pregnancies. Clin Perinatol. 2006;33:301–13.
9. Knopman J. Monozygotic twinning: an eight-year experience at a large IVF center. Fertil Steril. 2010;2:94.
10. Bebbington M. Selective reduction in multiple gestations. Best Pract Res Clin Obstet Gynaecol. 2014;28:239–47.
11. Kanhai HHH, van Rijssel EJC, Meerman RJ, Bennebroek GJ. Selective termination in quintuplet pregnancy during first trimester. Lancet. 1986;1:1447.
12. Jigal H, Ariel H, Jehoshua D, et al. Pregnancy outcome of early multifetal pregnancy reduction: triplets to twins versus triplets to singletons. Reprod BioMed Online. 2014;29:717–21.
13. Roni Z, Jigal H, Yossi B, Eran B, Keren Z, Natan A, et al. Pregnancy outcome after multifetal pregnancy reduction of triplets to twins versus reduction to singletons. Reprod BioMed Online. 2020;40:445–52.
14. Jigal H, Eran B, Ariel H, Jehoshua D, Shlomo L, Yoav Y, et al. Outcome of early versus late multifetal pregnancy reduction. Reprod BioMed Online. 2016;33:629–34.
15. Chaveeva P, Kosinski P, Puglia D, et al. Trichorionic and dichorionic triplet pregnancies at 10-14 weeks: outcome after embryo reduction compared to expectant management. Fetal Diagn Ther. 2013;34:199–205.
16. van de Mheen L, Everwijn SM, Haak MC, Manten GT, Zondervan HA, Knapen MF, et al. Outcome of multifetal pregnancy reduction in women with a Dichorionic Triamniotic triplet pregnancy to a singleton pregnancy: a retrospective Nationwide cohort study. Fetal Diagn Ther. 2016;40:94–9.
17. Tollenaar Lisanne SA, Femke S, Liesbeth L, Claire C, Mariano L, Sophie WA, et al. Spontaneous twin anemia polycythemia sequence: diagnosis, management, and outcome in an international cohort of 249 cases. Am J Obstet Gynecol. 2021;224(2):213.e1–213.e11.
18. Cai P, Ouyang Y, Gong F, Li X. Pregnancy outcomes of dichorionic triamniotic triplet pregnancies after in vitro fertilization-embryo transfer: multifoetal pregnancy reduction versus expectant management. BMC Pregnancy Childbirth. 2020;20:165.
19. Liu Y, Shen Y, Zhang H, Tang Y, Lu G, Gong F. Clinical outcomes of multifetal pregnancy reduction in trichorionic and dichorionic triplet pregnancies: a retrospective observational study. Taiwan J Obstet Gynecol. 2019;58:133–8.
20. Morlando M, Ferrara L, D'Antonio F, Lawin-O'Brien A, Sankaran S, Pasupathy D, et al. Dichorionic triplet pregnancies: risk of miscarriage and severe preterm delivery with fetal reduction versus expectant management. Outcomes of a cohort study and systematic review. BJOG. 2015;122:1053–60.
21. Chaveeva P, Peeva G, Pugliese SG, et al. Intrafetal laser ablation for embryo reduction from dichorionic triplets to dichorionic twins. Ultrasound Obstet Gynecol. 2017;50:632–4.
22. Papageorghiou AT, Avgidou K, Bakoulas V, et al. Risks of miscarriage and early preterm birth in trichorionic triplet pregnancies with embryo reduction versus expectant management: new data and systematic review.[J]. Hum Reprod. 2006;21:1912–7.
23. Wimalasundera RC. Selective reduction and termination of multiple pregnancies.[J]. Semin Fetal Neonatal Med. 2010;15:327–35.
24. Yaniv Z, Jigal H, Howard B, et al. Multifetal pregnancy reduction of triplets to twins compared with non-reduced triplets: a meta-analysis.[J]. Reprod BioMed Online. 2017;35:296–304.
25. Evans MI, Goldberg JD, Horenstein J, et al. Selective termination for structural, chromosomal, and mendelian anomalies: international experience. [J]. Am J Obstet Gynecol. 1999;181:893–7.
26. Lipitz S, Shulman A, Achiron R, et al. A comparative study of multifetal pregnancy reduction from triplets to twins in the first versus early second trimesters after detailed fetal screening.[J]. Ultrasound Obstet Gynecol. 2001;18:35–8.
27. Liu Y, Xietong W, Hongyan L, et al. Effects of the timing of selective reduction and finishing number of fetuses on the perinatal outcome in triplets: a single-center retrospective study.[J]. J Matern Fetal Neonatal Med. 2020;undefined:1–6.
28. Olivennes F, Doumerc S, Senat MV, Audibert F, Fanchin R, Frydman R. Evidence of early placental vascular anastomosis during selective embryo reduction in monozygotic twins. Fertil Steril. 2002;77:183–4.
29. Raval Donna B, Mary N, Iqbal Sara N, et al. Outcomes of Triplets reduced to Twins versus non-reduced Triplet Pregnancies.[J]. J Clin Gynecol Obstet. 2015;4:160–3.
30. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Munson ML. Births:final data for 2002. Natl Vital Stat Rep. 2003;52:1–113.
31. Bhide A, Sankaran S, Sairam S, Papageorghiou AT, Thilaganathan B. Relationship of intertwin crown–rump length discrepancy to chorionicity, fetal demise and birth weight discordance. Ultrasound Obstet Gynecol. 2009;34:131–5.
32. Athanasiadis AP, Zafrakas M, Tarlatzis BC, Vaitsi V, Mikos T, Bontis J. Multifetal pregnancy reduction in pregnancies with a monochorionic component. Fertil Steril. 2005;83:474–6.
33. Li R, Chen X, Yang S, Yang R, Ma C, Liu P, et al. Retain singleton or twins? Multifetal pregnancy reduction strategies in triplet pregnancies with monochorionic twins. Eur J Obstet Gynecol Reprod Biol. 2013;167:146–8.
34. Li Y, Yang D, Zhang Q. Dichorionic quadramniotic quadruple gestation with monochorionic triamniotic triplets after two embryos transfer and selective reduction to twin pregnancy: case report. Fertil Steril. 2009;92(2038):e13–5.
35. Ibérico G, Navarro J, Blasco L, et al. Embryo reduction of multifetal pregnancies following assisted reproduction treatment: a modification of the transvaginal ultrasound-guided technique. Hum Reprod. 2000;15:2228–33.
36. Oloyede Olufemi A, Faye I, Kehinde B. Spontaneous fetal reduction and early pregnancy complications in multiple pregnancies following in vitro fertilization. Int J Gynaecol Obstet. 2012;119(1):57–60.
37. van de Mheen L, Everwijn Sheila MP, Knapen Maarten FCM, Dick O, Melanie E, Manten Gwendolyn TR, et al. The effectiveness of multifetal pregnancy reduction in trichorionic triplet gestation. Am J Obstet Gynecol. 2014;211(5):536.e1–6.
38. Abbas A, Johnson M, Bersinger N, Nicolaides K. Maternal alpha-fetoprotein levels in multiple pregnancies. BJOG. 1994;101:156–8.
39. Eran W, Elad B, Ohad F, Ann D, Letizia S, Jacob B, et al. Placental histopathology differences and neonatal outcome in Dichorionic-Diamniotic as compared to Monochorionic-Diamniotic twin pregnancies. Reprod Sci. 2018;25(7):1067–72.
40. Song B, Wang Z, Chen Y, Wang C, Wei Z, He X, et al. Repeated triplets complicated by monochorionic diamniotic twins following assisted reproduction: a case report and literature review. BMC Pregnancy Childbirth. 2020;20:373.

Publisher's Note