Original Article

Effects of donor sperm on perinatal and neonatal outcomes resulting from in vitro fertilization-intracytoplasmic sperm injection and embryo transfer cycles: a retrospective cohort study

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Background: The impact of donor sperm on pregnancy outcomes is controversial. The aim of this study was to investigate whether donor sperm in in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) treatment could reduce the rate of live births or increase the incidence of adverse pregnancy outcomes and birth defects in neonates.

Methods: This single-centre, retrospective cohort study included 1,559 patients with infertility who received donor sperm at our hospital from 2015 to 2019. All the patients received fresh embryos and underwent first-cycle transfer. After propensity score matching, 4,677 controls who received their partners' sperm were matched at 1:3. Clinical pregnancy, perinatal, and neonatal outcomes were compared between the donor sperm and partner sperm groups.

Results: The embryo development was better in the donor sperm group than in the partner sperm group. The high-quality embryo and available embryo rates were significantly higher in the donor sperm group (P<0.05 for both groups). The rate of high-quality embryos transferred from the donor sperm group was higher than that from the partner sperm group (P<0.05). The clinical pregnancy (62.99% *vs.* 59.65%; P=0.02) and live birth (54.65% *vs.* 51.59%; P=0.036) rates were higher in the donor sperm group. After adjusting for confounding factors, no significant difference in live birth rates was observed between the two groups (adjusted P=0.057). The low birthweight (18.21% *vs.* 21.39%; P=0.023) and small for gestational age (SGA) (7.60% *vs.* 11.97%; P<0.001) rates were lower in the donor sperm group. To exclude the effect of multiple pregnancies, we evaluated neonatal outcomes of singleton pregnancies. No significant differences were noted in preterm and very preterm birth, SGA, mean birthweight, high birthweight, and low birth weight (LBW) and very low birth weight (VLBW) rates (P>0.05 for both groups). Further, no significant between group differences were observed in the ectopic pregnancy rate, early and late spontaneous abortion rates, gestational age, rate of large for gestational age (LGA), and neonatal defects.

Conclusions: Compared with partner sperm, donor sperm did not reduce live birth rate and did not increase neonatal LBW or low birth defects.

Keywords: Assisted reproductive technology (ART); donor sperm; neonatal outcomes; perinatal outcomes; pregnancy outcomes

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Introduction

Male fertility factors account for approximately 40% of all infertility cases (1). Among these factors, azoospermia accounts for approximately 10–15% of male infertility cases (2). After the birth of the first child conceived by frozen donor sperm in 1953 (3), the use of assisted reproductive technology (ART) and donor sperm gradually increased as treatment methods for male infertility (4). In China, ART with donor sperm is suitable for male patients with irreversible azoospermia, severe oligospermia, asthenozoospermia, teratospermia, and severe genetic diseases that cause infertility. Some studies have shown that ART with donor sperm is prone to obstetric complications, such as premature delivery (5-7), possibly because patients who use donor sperm have had no previous contact with donor paternal antigens, thus leading to an increase in the incidence of adverse pregnancy outcomes related to placental formation (8).

A systematic review and meta-analysis of 37 articles reported that ART with donor sperm was associated with a lower risk of ectopic pregnancy [relative risk (RR) =0.69] and higher risk of hypertension syndrome during pregnancy (RR =1.44), pre-eclampsia (RR =1.49), and small for gestational age (SGA) (RR =1.42) than ART with partner sperm (9). Some studies have shown that the incidence of pre-eclampsia with ART cycles is higher when donor sperm is used than when partner sperm is used (10,11). A study based on the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) database, including first ART cycles with 2,123 donor sperm and 42,799 partner sperm, showed that no significant differences were observed in the rates of spontaneous abortion, preterm birth, very preterm birth, low birth weight (LBW), and very low birth weight (VLBW) between the donor sperm and partner sperm groups and that the mean birth weight of the partner sperm group was significantly lower than that of the donor sperm group (8). This study included large data, and linear or logistic regression was performed to adjust for previously identified confounders, which effectively reduced errors attributable to sample size and increased the credibility of the findings (8). Logistic regression analysis was performed in a study published in 2018 to adjust for confounding factors for perinatal outcomes, and no significant differences in the risks of preterm birth, LBW, and high birth weight (HBW) were found after in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) with either donor sperm or partner sperm (12). To exclude any effect of multiple gestation on pregnancy outcomes, the two studies mentioned above only evaluated singleton pregnancies, and their research findings were similar. However, neither of these studies evaluated the impact on maternal complications during pregnancy, SGA, large for gestational age (LGA), or other related outcomes.

Many studies have evaluated intrauterine insemination with donor sperm; however, only few studies have examined IVF/ICSI with donor sperm (13-17). Furthermore, only some comprehensive studies have evaluated the pregnancy, perinatal, and neonatal outcomes of ART with donor sperm in China. Therefore, the aim of this single-center, retrospective cohort study was to evaluate the effects of donor sperm on pregnancy, perinatal, and neonatal outcomes after IVF/ICSI cycles in patients who received donor sperm at our hospital. We present the following article/case in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-21-5492/rc).

Methods

Study design

In this single-center, retrospective cohort study, we enrolled patients who visited the Affiliated Reproductive Hospital of Shandong University. From January 2015 to December 2019, 5,584 patients with infertility received donor sperm, and 81,618 patients with infertility received sperm from their partners. All the patients underwent fresh embryo transfer and IVF or ICSI treatment. To eliminate the possibility of maternal immune tolerance induced by prior donor sperm exposure, we further limited the final analysis to the first ART cycle. The exclusion criteria were donor oocytes, abnormal female chromosome structure, and patients with cancelled cycles.

A total of 1,559 patients using donor sperm and 4,677 patients using their partners' sperm were included and matched at 1:3. The matching criteria included maternal age, body mass index (BMI), years of infertility, basic follicle-stimulating hormone (FSH) level, basic luteinizing hormone (LH) level, basic estradiol (E2) level, partner's age, infertility type (primary or secondary), protocol for controlled ovarian hyper-stimulation [COH; long, short, gonadotropin-releasing hormone (GnRH) agonist protocol, ultra-long protocol, and other protocols, including the mini-stimulation and natural protocols], and reasons for infertility (polycystic ovary

syndrome, uterine factors, endometriosis, tubal factors, unexplained infertility, multifactorial infertility, male factors, and other reasons).

Donor sperm sources and principles

In the partner sperm group, the partner was allowed to provide semen by masturbation on the day of oocyte retrieval. In the donor sperm group, the frozen semen of the donor was thawed on the day of female oocyte collection. The frozen semen of the donor was evaluated according to its physical appearance. All donor sperm used at our hospital were obtained from the Human Sperm Bank of Shandong Province. The semen quality met the following relevant requirements: the donor blood type matched the partner's blood type; the same donor sperm could be used to fertilize up to five women; and donor sperm-assisted fertilization was performed with strict adherence to the relevant laws, regulations, and ethical principles. All the patients who received donor sperm did so voluntarily and provided informed consent to undergo donor sperm-assisted fertilization before surgery. All semen analyses were performed at the same andrology laboratory before the IVF/ICSI cycle.

COH, IVF, ICSI, and embryo transfer

The patient's age, anti-Müllerian hormone level, basic FSH level, BMI, other basic parameters, and their willingness and economic status were considered for the COH protocol. Commonly used protocols included the long, short, GnRH antagonist, ultra-long, natural cycle, or mini-stimulus protocols. The embryo score was obtained on the third day after fertilization and calculated based on the cytoplasmic fragment ratio and the number of blastomeres. One or two embryos were then selected for transplantation. The embryos continued to undergo blastocyst culture and were transplanted, or they were cryopreserved for thawing and subsequent re-transplantation. Day 3 (D3) high-quality embryos were scored according to the number of cells in the blastomere and the ratio of fragments: blastomeres comprised 7–10 cells or fusion embryos, and cell fragments were <30% (18). The embryos developed to day 5, and blastocyst assessment was then performed according to the Gardner scoring system (19). A high-quality blastocyst was defined as that having a comprehensive blastocyst cavity formation speed, inner cell mass, trophectoderm quality grade, and a blastocyst score ≥4 BC (20).

Luteal support was performed after oocyte retrieval and continued until the day of embryo transfer. If human chorionic gonadotropin was detected 14 days after transplantation, the progestin dosage was then gradually reduced until clinical pregnancy was confirmed.

Clinical pregnancy diagnosis and follow-up

At the first follow-up examination conducted 14 days after transplantation, pregnancy was confirmed. The second follow-up examination was conducted 30–35 days after transplantation to determine whether intrauterine pregnancy was established, and the number of foetuses present was recorded. The third follow-up examination was conducted 70–75 days after embryo transfer to determine foetal development. The fourth follow-up examination was conducted via telephone at 1 month after the expected date of delivery to determine maternal and infant health conditions.

Outcome measures

Our outcome measures included pregnancy, perinatal, and neonatal outcomes. Pregnancy outcomes included live birth, clinical pregnancy, biochemical pregnancy, preterm birth, overdue birth, ectopic pregnancy, early spontaneous abortion, and late spontaneous abortion rates.

Perinatal outcomes included the delivery method (vaginal birth or caesarean delivery) and maternal complications [gestational diabetes, gestational hypertension (blood pressure ≥140/90 mmHg after 20 weeks of gestation), preeclampsia, oligohydramnios, placenta previa, and placental abruption].

Neonatal outcomes included gestational age (weeks), preterm birth rate, very preterm birth rate, newborn sex (male or female), number of newborns (single births or multiple births), mean birth weight (kg), HBW, LBW, VLBW, LGA, SGA, and the incidents of birth defects (the central nervous system; eye, ear, face, and neck; circulatory system; respiratory system; cleft lip and palate; digestive system; genitourinary system; musculoskeletal system; other deformities; and chromosomal abnormalities). We defined SGA and LGA as birth weights <10th percentile and >90th percentile of the average body weight at the same gestational week, respectively (21). We defined preterm birth as birth between 28 and 37 weeks of gestation. We defined very preterm birth as birth between 28 and 33 weeks of gestation. HBW, LBW, and VLBW were defined as birth

weights of >4,000, <2,500, and <1,500 g, respectively.

Statistical analysis

All analyses were performed using IBM SPSS Statistics (version 26.0; IBM, Inc.) and R Studio. Categorical data were presented as frequencies and percentages; variables in these measures were compared between the groups using the chi-squared or Fisher's exact test. Ordinal categorical variables were analysed using the Mann-Whitney U test. Continuous data were presented as the mean ± standard deviation. All hypothesis tests were two-sided, and statistical significance was set at P<0.05. Binary logistic regression was used to adjust for confounding factors to further clarify the association of the sperm source with pregnancy outcomes and births. Adjustments were made for maternal age, BMI, years of infertility, basic FSH, LH, and E2 levels, partner's age, infertility type (primary or secondary), COH protocol, infertility reason, sperm quality before IVF/ICSI, and transferred embryo quality. The results were presented as odds ratios (ORs), adjusted odds ratios (aORs), and 95% confidence intervals (CIs).

Ethics statement

The study conformed to the provisions of the Declaration of Helsinki as revised in 2013. This study was a retrospective analysis of clinical practice outcomes. Our data analysis was approved by the Institutional Review Board of the Reproductive Hospital Affiliated to Shandong University (2021; IRB No. 116). Written informed consent was obtained from all participants at the time of presentation for IVF/ICSI.

Results

From 2015 to 2019, 5,584 patients with infertility received donor sperm, and 81,618 patients with infertility received sperm from their partners. After considering the exclusion criteria, a total of 1,559 patients who received donor sperm (donor sperm group) were included and matched 1:3 with 4,677 patients who received sperm from their partners (partner sperm group).

Comparison of the basic characteristics of the two groups

The demographic and main treatment characteristics of the patients are listed in *Table 1*. There were no significant differences in maternal age, BMI, years of infertility, basic FSH, LH, and E2 levels, AFC, partner's age, infertility type, or cause of female infertility between the two groups. The use of GnRH agonist short protocol (21.0% *vs.* 24.3%; P=0.007) was lower in the donor sperm group than in the partner sperm group. No significant differences were noted in the remaining ovarian stimulation protocols between the groups. Uterine (1.2% *vs.* 0.4%; P<0.001), multifactorial (48.1% *vs.* 43.0%; P<0.001), and male (32.5% *vs.* 24.2%; P<0.001) factors causing infertility were observed more frequently in the donor sperm group than in the partner sperm group. Tubal (15.3% *vs.* 20.9%; P<0.001), unexplained (0.3% *vs.* 1.8%; P<0.001), and other (1.3% *vs.* 8.7%; P<0.001) factors causing infertility were observed less often in the donor sperm group than in the partner sperm group. There were no significant differences in the incidence of polycystic ovary syndrome and endometriosis as causes of infertility. We compared the sperm quality of the two groups before IVF/ICSI treatment. The thawed donor semen volume was 1 mL, and the average semen volume of the partner sperm group was 2.52±1.70 mL. The sperm concentration [(50.01±7.20)×10^6/mL *vs.* (36.02±24.13)×10^6/mL; P<0.001], total sperm motility rate (49.55±7.01 *vs.* 35.77±23.79; P<0.001), and sperm forward motility rate (grade a + grade b) (38.17±6.84 *vs.* 26.88±19.06; P<0.001) were significantly higher in the donor sperm group than in the partner sperm group. The sperm quality of the donor sperm group was significantly better than that of the partner sperm group. Both groups were mainly treated by IVF.

Comparison of embryonic development between groups

Table 2 presents details of the embryonic development that occurred in both the groups. The number of follicles >1.4 cm on the human chorionic gonadotropin trigger day (P=0.03), number of oocytes retrieved (P=0.001), number of high-quality embryos (P=0.001), high-quality embryo rate (58.25% *vs.* 56.34%; P=0.001), number of embryos available (P<0.001), and available embryo rate (65.58% *vs.* 59.99%; P<0.001) were higher in the donor sperm group than in the partner sperm group. However, the number of two pronuclei fertilizations (P=0.002) in the donor sperm group were lower than those in the partner sperm group. Most patients choose to transfer two embryos. We divided the transplanted embryos into high-quality and non-high-quality embryos according to the laboratory rating. The rate of high-quality embryos transplanted at D3 (95.59% *vs.* 94.05%; P=0.005) and that of high-quality blastocysts transplanted at day 5 (D5) (95.14% *vs.* 90.13%; P=0.004)

Table 1 Comparison of basic characteristics of the two groups

Characteristics	Donor sperm group (n=1,559)	Partner sperm group (n=4,677)	P value
Age, years	30.54±4.44	30.55±4.73	0.91
BMI, kg/m^2	23.56±3.47	23.67±3.76	0.757
Infertility duration, years	4.82±3.33	4.78±3.42	0.662
Basic FSH, IU/L	6.86±2.12	6.91±2.30	0.393
Basic LH, IU/L	6.19±5.55	5.91±4.58	0.824
Basic E2, pg/mL	54.63±97.25	46.68±63.90	0.579
Antral follicle count	13.66±5.89	13.95±7.21	0.337
Age of the husband, years	31.49±4.75	31.54±5.12	0.356
Infertility type, n (%)			0.429
Primary infertility rate	1,097 (70.4)	3,340 (71.4)	
Secondary infertility rate	462 (29.6)	1,337 (28.6)	
Ovarian stimulation protocol, n (%)			
GnRH agonist, long	818 (52.5)	2,371 (50.7)	0.225
GnRH agonist, short	327 (21.0)	1,136 (24.3)	0.007
GnRH antagonist	338 (21.7)	891 (19.1)	0.251
GnRH agonist, ultra-long	55 (3.5)	184 (3.9)	0.469
Others	21 (1.3)	95 (2.0)	0.083
Cause of female infertility, n (%)			
PCOS	14 (0.9)	28 (0.6)	0.211
Uterine factors	19 (1.2)	19 (0.4)	<0.001
Endometriosis	6 (0.4)	18 (0.4)	>0.99
Tubal factors	239 (15.3)	979 (20.9)	<0.001
Unexplained factors	5 (0.3)	82 (1.8)	<0.001
Multifactorial	750 (48.1)	2,012 (43.0)	<0.001
Male factors	506 (32.5)	1,131 (24.2)	<0.001
Other factors	20 (1.3)	408 (8.7)	<0.001
Semen volume, mL	1±0	2.52±1.70	<0.001
Concentration, 10^6/mL	50.01±7.20	36.02±24.13	<0.001
Motility, %	49.55±7.01	35.77±23.79	<0.001
Sperm forward motility rate (grade a + grade b), %	38.17±6.84	26.88±19.06	<0.001
Fertility method, n (%)			<0.001
IVF	1,538 (98.65)	2,639 (56.43)	
ICSI	21 (1.35)	2,038 (43.57)	

BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; E2, estradiol; GnRH, gonadotropin-releasing hormone; PCOS, polycystic ovary syndrome; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection.

Table 2 Comparison of embryo development between the two groups

Variables	Donor sperm group	Partner sperm group	P value
Endometrial thickness on hCG trigger day, cm	1.10±0.19	1.10±0.19	0.995
No. of follicles >1.4 cm on hCG trigger day	9.28±3.93	9.02±4.03	0.03
No. of oocytes	9.37±4.21	8.97±4.27	0.001
No. of 2PN fertilizations	5.05±3.70	5.37±3.55	0.002
Fertilization rate, n (%)	9,468/14,609 (64.81)	26,584/41,960 (63.36)	<0.001
No. of high-quality embryo	3.53±2.58	3.20±2.34	0.001
High-quality embryo rate, n (%)	5,515/9,468 (58.25)	14,977/26,584 (56.34)	0.001
No. of embryos available	4.60±2.91	4.07±2.67	<0.001
Available embryo rate, n (%)	6,209/9,468 (65.58)	15,948/26,584 (59.99)	<0.001
No. of embryos transferred, n (%)			–
One embryo	454 (29.1)	1,319 (28.2)	
Two embryos	1,105 (70.9)	3,358 (71.8)	
The quality of embryo transferred on D3, n (%)			0.005
Rate of D3 high-quality embryos transferred	2,212/2,314 (95.59)	6,673/7,095 (94.05)	
Rate of D3 non-high-quality embryos transferred	102/2,314 (4.41)	422/7,095 (5.95)	
The quality of blastocysts transferred on D5, n (%)			0.004
Rate of D5 high-quality blastocyst transferred	333/350 (95.14)	849/942 (90.13)	
Rate of D5 non-high-quality blastocyst transferred	17/350 (4.86)	93/942 (9.87)	

hCG, human chorionic gonadotropin; 2PN, two pronuclei; D3, day 3; D5, day 5.

were significantly higher in the donor sperm group than in the partner sperm group. The results indicated that the embryo development ability was higher in the donor sperm group than in the partner sperm group.

Comparison of pregnancy outcomes between groups

Furthermore, the live birth rate (54.65% *vs.* 51.69%; P=0.036; OR =1.131) and clinical pregnancy rate (62.99% *vs.* 59.65%; P=0.02; OR =1.151) of the donor sperm group were higher than those of the partner sperm group. There were no significant differences in the biochemical pregnancy (6.99% *vs.* 7.23%; P=0.755), preterm birth (7.89% *vs.* 9.02%; P=0.170), overdue birth (0.06% *vs.* 0.09%; P=0.797), ectopic pregnancy (0.81% *vs.* 1.18%; P=0.341), early spontaneous abortion (10.08% *vs.* 10.14%; P=0.956), or late spontaneous abortion (2.34% *vs.* 2.19%; P=0.776) rates between the groups.

After adjusting for maternal age, BMI, infertility years, basic FSH, LH, and E2 levels, partner's age, AFC, infertility type, COH protocol, reasons for infertility, sperm quality before IVF/ICSI, and transferred embryo quality, the donor sperm group had a higher clinical pregnancy rate (adjusted P=0.009; aOR =1.215) than the partner sperm group. There was no significant difference in the live birth rate between the two groups (adjusted P=0.057; aOR =1.149). Moreover, no significant differences were noted in the biochemical pregnancy, ectopic pregnancy, early spontaneous abortion, or late spontaneous abortion rates between the groups (*Table 3*).

Comparison of obstetric outcomes between groups

Regardless of whether donor sperm or partner sperm was used, pregnant women chose to undergo caesarean delivery more frequently than vaginal delivery, however, there was no significant difference between the groups (P=0.834). The incidence of gestational diabetes (8.57% *vs.* 6.38%; P=0.031) in the donor sperm group was higher than that in the partner sperm group. There were no

Table 3 Comparison of pregnancy outcomes between the donor and partner sperm groups

Outcomes	Donor sperm group	Partner sperm group	P value	Crude OR (95% CI)	Adjusted P value	Adjusted OR (95% CI)
Clinical pregnancy, n (%)	982 (62.99)	2,790 (59.65)	0.02	1.151 (1.023–1.296)	0.009	1.215 (1.050–1.407)
Live birth, n (%)	852 (54.65)	2,413 (51.59)	0.036	1.131 (1.008–1.269)	0.057	1.149 (0.996–1.325)
Biochemical pregnancy, n (%)	109 (6.99)	338 (7.23)	0.755	0.965 (0.771–1.207)	0.424	0.895 (0.681–1.175)
Preterm birth, n (%)	123 (7.89)	422 (9.02)	0.170	0.864 (0.700–1.065)	0.476	0.91 (0.703–1.179)
Overdue birth, n (%)	1 (0.06)	4 (0.09)	0.797	0.750 (0.084–6.714)	0.594	2.356 (0.101–54.936)
Ectopic pregnancy, n (%)	8 (0.81)	33 (1.18)	0.341	0.686 (0.316–1.491)	0.191	0.545 (0.219–1.354)
Early spontaneous abortion, n (%)	99 (10.08)	283 (10.14)	0.956	0.993 (0.780–1.264)	0.816	1.035 (0.777–1.379)
Late spontaneous abortion, n (%)	23 (2.34)	61 (2.19)	0.776	1.073 (0.660–1.743)	0.419	1.257 (0.722–2.189)

OR, odds ratio; CI, confidence interval.

Table 4 Comparison of perinatal outcomes between the donor and partner sperm groups

Outcomes	Donor sperm group (852 pregnancies)	Partner sperm group (2,413 pregnancies)	P value
Delivery method, n (%)			0.834
Vaginal birth	226 (26.53)	649 (26.90)	
Cesarean delivery	626 (73.47)	1,764 (73.10)	
Maternal complications, n (%)			
Gestational diabetes	73 (8.57)	154 (6.38)	0.031
Hypertension syndrome during pregnancy	49 (5.75)	136 (5.64)	0.901
Preeclampsia	5 (0.59)	13 (0.54)	0.87
Oligohydramnios	10 (1.17)	19 (0.79)	0.302
Placenta previa	4 (0.47)	19 (0.79)	0.476
Placental abruption	3 (0.35)	6 (0.25)	0.709

significant differences in the incidence of hypertension syndrome during pregnancy (5.75% *vs.* 5.64%; P=0.901), pre-eclampsia (0.59% *vs.* 0.54%; P=0.87), oligohydramnios (1.17% *vs.* 0.79%; P=0.302), placenta previa (0.47% *vs.* 0.79%; P=0.476), or placental abruption (0.35% *vs.* 0.25%; P=0.709) between the two groups (*Table 4*).

Comparison of perinatal outcomes between groups

Regardless of the sperm source, the birth rate of male newborns was higher than that of female newborns, however, the difference between the groups was not significant (P=0.997). Single births occurred more frequently than multiple births in both the donor sperm and partner sperm groups, nevertheless, there was no significant difference between the two groups (P=0.653). One set of twins from the donor sperm group was lost to follow-up; therefore, the sex and birth weight of the two newborns were unknown. The birth weights of 18 newborns lost to follow-up in the partner sperm group were also unknown. Finally, we included the birth weights of 1,131 newborns in the donor sperm group and 3,165 in the partner sperm group. The LBW (18.21% *vs.* 21.39%; P=0.023) and SGA (7.60% *vs.* 11.97%; P<0.001) rates of the donor sperm group were lower than those of the partner sperm group. There was no significant difference in the mean birth weight (3.00±0.63 *vs.* 2.97±0.66 kg; P=0.116), gestational age (38.51±1.99 *vs.* 38.37±2.12 weeks; P=0.081), HBW rate

Table 5 Comparison of perinatal outcomes between the donor and partner sperm groups

Outcomes	Donor sperm group	Partner sperm group	P value
Gestational age, weeks	38.51±1.99	38.37±2.12	0.081
Newborn sex, n (%)			0.997
Male	573/1,134 (50.53)	1,611/3,183 (50.61)	
Female	561/1,134 (49.47)	1,572/3,183 (49.39)	
No. of newborns, n (%)			0.653
Single birth	573/852 (67.25)	1,643/2,413 (68.09)	
Multiple births	279/852 (32.75)	770/2,413 (31.91)	
Mean birth weight, kg	3.00±0.63	2.97±0.66	0.116
HBW, n (%)	41/1,131 (3.63)	148/3,165 (4.68)	0.139
LBW, n (%)	206/1,131 (18.21)	677/3,165 (21.39)	0.023
VLBW, n (%)	15/1,131 (1.33)	48/3,165 (1.52)	0.648
LGA, n (%)	142/1,131 (12.56)	441/3,165 (13.93)	0.245
SGA, n (%)	86/1,131 (7.60)	379/3,165 (11.97)	<0.001
Stillbirth, n	0	4	–

HBW, high birth weight; LBW, low birth weight; VLBW, very low birth weight; LGA, large for gestational age; SGA, small for gestational age.

(3.63% *vs.* 4.68%; P=0.139), VLBW rate (1.33% *vs.* 1.52%; P=0.648), or LGA rate (12.56% *vs.* 13.93%; P=0.245) between the groups. Four stillbirths occurred in the partner sperm group, and no stillbirths occurred in the donor sperm group (*Table 5*).

Comparison of perinatal outcomes of single pregnancies between groups

To further verify the influence of the sperm source on birth, we excluded patients with multiple pregnancies. There were no significant differences in gestational age (39.31±1.45 *vs.* 39.21±1.61 weeks; P=0.185), mean birth weight (3.41±0.49 *vs.* 3.37±0.52 kg; P=0.19), HBW rate (7.16% *vs.* 8.70%; P=0.249; OR =0.809), LBW rate (2.97% *vs.* 4.11%; P=0.223; OR =0.714), VLBW rate (0.17% *vs.* 0.55%; P=0.274; OR =0.315), LGA rate (22.51% *vs.* 22.30%; P=0.918; OR =1.012), SGA rate (4.54% *vs.* 6.50%; P=0.091; OR =0.684), preterm birth rate (4.89% *vs.* 5.64%; P=0.496; OR =0.860), or very preterm birth rate (0.52% *vs.* 0.98%; P=0.317; OR =0.532) between the groups. After adjusting for potential confounders, there were no significant differences in the HBW rate (adjusted P=0.317; aOR =0.824), LBW rate (adjusted P=0.191; aOR =0.684), VLBW rate (adjusted P=0.182; aOR =0.198), LGA rate (adjusted P=0.746; aOR =1.041), SGA rate (adjusted P=0.065; aOR =0.650), preterm birth rate (adjusted P=0.430; aOR =0.830), and very preterm birth rate (adjusted P=0.271; aOR =0.477) between the groups (*Table 6*).

Comparison of birth defects between groups

Congenital malformations, modifications, and chromosomal abnormalities (Q00–Q99) as classified by the International Statistical Classification of Diseases and Related Health Problems (ICD-10) were observed. In the donor sperm group, there were 3 cases of central nervous system abnormalities; 2 cases of eye, ear, face, and neck abnormalities; 3 cases of circulatory system abnormalities; 10 cases of genitourinary system abnormalities; 2 cases of musculoskeletal system abnormalities; and 8 cases of other abnormalities. In the partner sperm group, there were 4 cases of central nervous system abnormalities; 6 cases of eye, ear, face, and neck abnormalities; 16 cases of circulatory system abnormalities; 3 cases of respiratory system abnormalities; 2 cases of cleft lip and palate; 3 cases of digestive system abnormalities; 15 cases of genitourinary system abnormalities; 3 cases of musculoskeletal system abnormalities; 11 cases of other abnormalities; and

Table 6 Comparison of single gestation outcomes between the donor and partner sperm groups

Outcomes	Donor sperm group (n=573)	Partner sperm group (n=1,632)	P value	Crude OR (95% CI)	Adjusted P value	Adjusted OR (95% CI)
Gestational age, weeks	39.31±1.45	39.21±1.61	0.185	–	–	–
Mean birth weight, kg	3.41±0.49	3.37±0.52	0.19	–	–	–
HBW, n (%)	41 (7.16)	142 (8.70)	0.249	0.809 (0.563–1.161)	0.317	0.824 (0.565–1.204)
LBW, n (%)	17 (2.97)	67 (4.11)	0.223	0.714 (0.416–1.227)	0.191	0.684 (0.387–1.208)
VLBW, n (%)	1 (0.17)	9 (0.55)	0.274	0.315 (0.040–2.494)	0.182	0.198 (0.018–2.136)
LGA, n (%)	129 (22.51)	364 (22.30)	0.918	1.012 (0.806–1.271)	0.746	1.041 (0.816–1.329)
SGA, n (%)	26 (4.54)	106 (6.50)	0.091	0.684 (0.441–1.062)	0.065	0.650 (0.412–1.027)
Preterm birth, n (%)	28 (4.89)	92 (5.64)	0.496	0.860 (0.557–1.328)	0.430	0.830 (0.523–1.318)
Very preterm birth, n (%)	3 (0.52)	16 (0.98)	0.317	0.532 (0.154–1.831)	0.271	0.477 (0.127–1.784)

OR, odds ratio; CI, confidence interval; HBW, high birth weight; LBW, low birth weight; VLBW, very low birth weight; LGA, large for gestational age; SGA, small for gestational age.

Table 7 Comparison of neonatal birth defects between the donor and partner sperm groups

Outcomes	Donor sperm group	Partner sperm group	P value
Central nervous system (Q00–Q07)	3	4	0.481
Eye, ear, face, and neck (Q10–Q18)	2	6	
Circulatory system (Q20–Q28)	3	16	
Respiratory system (Q30–Q34)	0	3	
Cleft lip and palate (Q35–Q37)	0	2	
Digestive system (Q38–Q45)	0	3	
Genitourinary system (Q50–Q64)	10	15	
Musculoskeletal system (Q65–Q79)	2	3	
Other deformities (Q80–Q89)	8	11	
Chromosomal abnormality (Q90–Q99)	0	4	
Total, n (%)	28/1,131 (2.48)	67/3,165 (2.12)	

4 cases of chromosomal abnormalities. No significant difference was noted in the incidence of birth defects between the donor and partner sperm groups (2.48% *vs.* 2.12%; P=0.481) (*Table* 7).

Discussion

This study investigated whether donor sperm adversely affects the pregnancy, obstetric, and neonatal outcomes of patients with infertility and found that the live birth and clinical pregnancy rates were higher in the donor sperm group than in the partner sperm group. However, after adjusting for confounding factors, there were no evident differences in the live birth rate between the two groups. The LBW and SGA rates of the donor sperm group were lower than those of the partner sperm group when multiple pregnancies were excluded. However, there was no significant difference between the two groups. We did not observe increased risks of hypertensive disorders during pregnancy, pre-eclampsia, or birth defects in the donor sperm group.

In our study, the retrieved oocyte and embryo development were better in the donor sperm group than

in the partner sperm group. The number of follicles >1.4 cm on the human chorionic gonadotropin trigger day, number of oocytes, number and rate of high-quality embryos, and number and rate of embryos available were higher in the donor sperm group than in the partner sperm group. In addition, we compared the embryonic development quality of the transferred embryos between the two groups. In the embryos transferred from the donor sperm group, the D3 high-quality embryo rate and D5 high-quality blastocyst rate were higher than those in the partner sperm group. The quality of the transferred embryos in the donor sperm group was higher than that in the partner sperm group. Some studies have shown that male infertility factors can affect the ability of the embryo to develop (22,23). Sperm factors affecting early embryonic development include paternal genetic and paternal epigenetic factors. Paternal genetic factors include sperm chromosomal abnormalities and sperm DNA loss. Paternal epigenetic factors include sperm DNA methylation, sperm histone modification, sperm chromatin advanced structural packaging and sperm-derived ncRNA, and other factors (24). Decreased sperm motility and impaired sperm morphology have been reported to lead to decreased embryonic development and embryo quality (25). In our study, the sperm concentration and sperm motility before IVF/ICSI treatment were higher in the donor sperm group than in the partner sperm group, which also indicated that high-quality sperm potentially promoted the development of embryos.

Our results showed that the donor sperm group was not associated with a reduction in the live birth rate compared with that of the partner sperm group (54.65% *vs.* 51.59%). A previous study found that donor sperm can partially compensate for the age-related decline in oocyte development because higher-quality paternal genetic material can be used to fertilize oocytes, thereby increasing the live birth rate of ICSI cycles in older patients (26). Moreover, a study of intrauterine insemination using donor sperm and partner sperm in 2018 reported no significant difference in the live birth rates between the groups (16). Smith *et al.* and Gerkowicz *et al.* compared the effects of donor sperm on pregnancy outcomes after IVF/ICSI and found no difference in the live birth rates between the donor and partner sperm groups (27,28). According to the existing literature, whether donor sperm potentially improves the live birth rate remains controversial. When we compared the two groups after adjusting for confounders, we did not find donor sperm to be associated with a decrease in live birth rates.

In our study, the clinical pregnancy rate of the donor sperm group was higher than that of the partner sperm group (62.99% *vs.* 59.65%), this might have occurred because the sperm quality was higher in the donor sperm group than in the partner sperm group (29,30). Dong *et al.* (31) studied artificial insemination cycles using partner and donor sperm and found that the clinical pregnancy rate of the donor sperm group was higher than that of the partner sperm group (27.5% *vs.* 10.8%). Frank *et al.* (32) compared the clinical outcomes of women aged ≥38 years who underwent artificial insemination using partner sperm and donor sperm and found that the clinical pregnancy rate of the donor sperm group was higher than that of the partner sperm group. However, the difference between the groups was not significant (8% *vs.* 5.8%). The results of these studies are consistent with our findings. In our study, the sperm quality and embryonic development of the donor sperm group were better than those of the partner sperm group. Therefore, the clinical pregnancy rate of the donor sperm group was higher than that of the partner sperm group.

Previous studies have indicated that a potential mechanism of pre-eclampsia is abnormal maternal immunity to paternal antigens and that repeated exposure to antigens in paternal semen before pregnancy can effectively reduce its occurrence (10,33-35). Other studies have speculated that donor sperm may increase the incidence of pre-eclampsia (11,14,36-39). In our study, although the incidence of pre-eclampsia was slightly higher in the donor sperm group than in the partner sperm group (0.59% *vs.* 0.54%), the difference was not statistically significant. Donor sperm was not found to increase the incidence of pre-eclampsia.

The LBW rate was higher in the donor sperm group (18.21% *vs.* 21.23%). Some studies have revealed an increased risk of LBW for patients who chose to use donor sperm for intrauterine insemination (6,40). Other studies have shown that there is no increased risk of LBW when donor sperm is used for intrauterine insemination in patients with infertility (12,16). Kamath *et al.* (12) compared the LBW rates of IVF/ICSI patients who used donor sperm and partner sperm and found that the donor sperm group had a lower LBW rate. Gaudoin *et al.* (41) also found that the LBW rate was lower in neonates conceived with donor sperm than in those conceived with partner sperm (11.4% *vs.* 22.7%), these results are consistent with our findings.

In our study, the donor sperm group had a lower rate of preterm birth than the partner sperm group (7.89% *vs.* 9.02%), which might have contributed to the higher LBW rate in the partner sperm group than in the donor sperm group (15).

A large study investigating artificial insemination performed in Copenhagen showed that women receiving donor sperm had a higher SGA than those receiving partner sperm (2.7% *vs.* 3.83%) (13). However, that study focused on explaining the effect of ovarian stimulation on SGA and did not explain the effect of donor sperm on SGA. In that study, the preterm birth and LBW rates in the donor sperm group were higher than those in the partner sperm group, which increased the SGA rates. Two other studies with smaller sample sizes did not find a statistically significant difference in the SGA rates of the donor sperm group and partner sperm group (42,43). Our results indicate that the SGA was lower in the donor sperm group than in the partner sperm group (7.60% *vs.* 11.97%; P<0.001). We ruled out the effects of multiple pregnancies. Further, we showed that there were no significant differences in mean birth weight, the incidence of HBW, LBW, or VLBW, LGA or SGA, and preterm or very preterm birth rates between the groups. There were also no significant differences after adjusting for confounding factors. There were many factors that influenced SGA, however, few studies have evaluated the effects of donor sperm on SGA. The explanation of our results regarding SGA may be attributed to the insufficient sample size in our study. Multicenter, prospective studies with larger sample sizes should be performed in the future to confirm these results.

Whether IVF and ICSI increase birth defect rates remains controversial worldwide (44-46). One study showed that artificial insemination with donor sperm did not increase the incidence of birth defects in offspring (47). A recent meta-analysis showed that newborns conceived using donor sperm had a higher incidence of birth defects than newborns conceived without ART (40). Some studies have found that malformations of the cardiovascular and musculoskeletal systems are the most frequent birth defects observed in newborns conceived with IVF/ICSI, followed by cleft lip and palate and defects of the genitourinary and central nervous systems (46,48). In our study, the highest incidence of birth defects was observed in the genitourinary and circulatory systems. However, there were no significant differences in the incidence of birth defects observed in the donor and partner sperm groups. Our results did not indicate that donor sperm increased the incidence of birth defects in offspring.

Limitations

This study has some limitations. Our data were limited to patients visiting our hospital from 2015 to 2019, which resulted in a small sample size. Further, our study was subject to the inherent flaws of retrospective studies. Therefore, multi-centre, prospective studies with large sample sizes are necessary to verify the effects of donor sperm on pregnancy outcomes of patients with infertility. Another limitation of this study was that the women's smoking history might not have been accurately discerned because some patients could have concealed their tobacco use and alcohol consumption. Finally, our hospital is a fertility centre, a comparison with patients who conceive without ART was not possible.

Conclusions

Our results suggest that donor sperm did not (I) affect embryonic development or (II) have adverse effects on pregnancy, perinatal, and neonatal outcomes or (III) increase the incidence of neonatal birth defects. The study suggests that the use of donor sperm is safe. The results of this study provide clinical support for patients with infertility using donor sperm and can alleviate patients' concerns about the outcomes of pregnancies conceived using donor sperm.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-21-5492/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-21-5492/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The retrospective study of clinical practice outcomes and data analysis were approved by the Institutional Review Board of the Reproductive Hospital Affiliated to Shandong University (2021; No. 116). Written informed consent was obtained from all participants at the time of presentation for IVF/ICSI.

References

1. Kumar N, Singh AK. Trends of male factor infertility, an important cause of infertility: A review of literature. J Hum Reprod Sci 2015;8:191-6.
2. Streda R, Mardesic T, Sobotka V, et al. Comparison of different starting gonadotropin doses (50, 75 and 100 IU daily) for ovulation induction combined with intrauterine insemination. Arch Gynecol Obstet 2012;286:1055-9.
3. Steinberger E, Smith KD. Artificial insemination with fresh or frozen semen. A comparative study. JAMA 1973;223:778-83.
4. De Geyter C, Calhaz-Jorge C, Kupka MS, et al. ART in Europe, 2015: results generated from European registries by ESHRE. Hum Reprod Open 2020;2020:hoz038.
5. Henningsen AA, Wennerholm UB, Gissler M, et al. Risk of stillbirth and infant deaths after assisted reproductive technology: a Nordic study from the CoNARTaS group. Hum Reprod 2014;29:1090-6.
6. Sunkara SK, La Marca A, Seed PT, et al. Increased risk of preterm birth and low birthweight with very high number of oocytes following IVF: an analysis of 65 868 singleton live birth outcomes. Hum Reprod 2015;30:1473-80.
7. Qin J, Liu X, Sheng X, et al. Assisted reproductive technology and the risk of pregnancy-related complications and adverse pregnancy outcomes in singleton pregnancies: a meta-analysis of cohort studies. Fertil Steril 2016;105:73-85.e1-6.
8. Yu B, Fritz R, Xie X, et al. The impact of using donor sperm in assisted reproductive technology cycles on perinatal outcomes. Fertil Steril 2018;110:1285-9.
9. Allen CP, Marconi N, McLernon DJ, et al. Outcomes of pregnancies using donor sperm compared with those using partner sperm: systematic review and meta-analysis. Hum Reprod Update 2021;27:190-211.
10. Dekker GA, Robillard PY, Hulsey TC. Immune maladaptation in the etiology of preeclampsia: a review of corroborative epidemiologic studies. Obstet Gynecol Surv 1998;53:377-82.
11. González-Comadran M, Urresta Avila J, Saavedra Tascón A, et al. The impact of donor insemination on the risk of preeclampsia: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2014;182:160-6.
12. Kamath MS, Antonisamy B, Selliah HY, et al. Perinatal outcomes following IVF with use of donor versus partner sperm. Reprod Biomed Online 2018;36:705-10.
13. Malchau SS, Loft A, Henningsen AK, et al. Perinatal outcomes in 6,338 singletons born after intrauterine insemination in Denmark, 2007 to 2012: the influence of ovarian stimulation. Fertil Steril 2014;102:1110-6.e2.
14. Kyrou D, Kolibianakis EM, Devroey P, et al. Is the use of donor sperm associated with a higher incidence of preeclampsia in women who achieve pregnancy after intrauterine insemination? Fertil Steril 2010;93:1124-7.
15. Huang D, Song S, Liao A. Short-term safety evaluation of the offspring conceived by 7272 artificial insemination cycles with donor spermatozoon. Andrologia 2016;48:817-23.
16. Chen L, Zhu L, Cai C, et al. Clinical and neonatal outcomes of intrauterine insemination with frozen donor sperm. Syst Biol Reprod Med 2018;64:240-5.
17. Guan HT, Zheng Y, Wang JJ, et al. Relationship between donor sperm parameters and pregnancy outcome after intrauterine insemination: analysis of 2821 cycles in 1355 couples. Andrologia 2016;48:29-36.
18. Puissant F, Van Rysselberge M, Barlow P, et al. Embryo

scoring as a prognostic tool in IVF treatment. Hum Reprod 1987;2:705-8.
19. Gardner DK, Lane M, Stevens J, et al. Blastocyst score affects implantation and pregnancy outcome: towards a single blastocyst transfer. Fertil Steril 2000;73:1155-8.
20. Mukaida T, Nakamura S, Tomiyama T, et al. Vitrification of human blastocysts using cryoloops: clinical outcome of 223 cycles. Hum Reprod 2003;18:384-91.
21. Capital Institute of Pediatrics; Coordinating Study Group of Nine Cities on the Physical Growth and Development of Children. Growth standard curves of birth weight, length and head circumference of Chinese newborns of different gestation. Zhonghua Er Ke Za Zhi 2020;58:738-46.
22. Cai H, Gordts S, Sun J, et al. Reproductive outcomes with donor sperm in couples with severe male-factor infertility after intracytoplasmic sperm injection failures. J Assist Reprod Genet 2020;37:1883-93.
23. Colaco S, Sakkas D. Paternal factors contributing to embryo quality. J Assist Reprod Genet 2018;35:1953-68.
24. Zhou JT, Ma H, Zhang BB, et al. Sperm factors affecting early embryonic development. J Reprod Med 2019;28:1264-70.
25. Miller JE, Smith TT. The effect of intracytoplasmic sperm injection and semen parameters on blastocyst development in vitro. Hum Reprod 2001;16:918-24.
26. Mignini Renzini M, Dal Canto M, Guglielmo MC, et al. Sperm donation: an alternative to improve post-ICSI live birth rates in advanced maternal age patients. Hum Reprod 2021;36:2148-56.
27. Smith ADAC, Tilling K, Nelson SM, et al. Live-Birth Rate Associated With Repeat In Vitro Fertilization Treatment Cycles. JAMA 2015;314:2654-62.
28. Gerkowicz SA, Crawford SB, Hipp HS, et al. Assisted reproductive technology with donor sperm: national trends and perinatal outcomes. Am J Obstet Gynecol 2018;218:421.e1-421.e10.
29. Soria M, Pradillo G, García J, et al. Pregnancy predictors after intrauterine insemination: analysis of 3012 cycles in 1201 couples. J Reprod Infertil 2012;13:158-66.
30. Marik J. Cross-over study of intrauterine and intracervical insemination. Fertil Steril 2002;77:426.
31. Dong Fl, Sun Yp, Su Yc, et al. Relationship between processed total motile sperm count of husband or donor semen and pregnancy outcome following intrauterine insemination. Syst Biol Reprod Med 2011;57:251-5.
32. Frank R, Steiner N, Al Shatti M, et al. Outcomes of donor versus partner sperm in intrauterine insemination in women aged 38 years and older. Int J Gynaecol Obstet 2022;156:516-20.
33. Sibai BM. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol 2005;105:402-10.
34. Saftlas AF, Rubenstein L, Prater K, et al. Cumulative exposure to paternal seminal fluid prior to conception and subsequent risk of preeclampsia. J Reprod Immunol 2014;101-102:104-10.
35. Saftlas AF, Levine RJ, Klebanoff MA, et al. Abortion, changed paternity, and risk of preeclampsia in nulliparous women. Am J Epidemiol 2003;157:1108-14.
36. Need JA, Bell B, Meffin E, et al. Pre-eclampsia in pregnancies from donor inseminations. J Reprod Immunol 1983;5:329-38.
37. Smith GN, Walker M, Tessier JL, et al. Increased incidence of preeclampsia in women conceiving by intrauterine insemination with donor versus partner sperm for treatment of primary infertility. Am J Obstet Gynecol 1997;177:455-8.
38. Salha O, Sharma V, Dada T, et al. The influence of donated gametes on the incidence of hypertensive disorders of pregnancy. Hum Reprod 1999;14:2268-73.
39. Hoy J, Venn A, Halliday J, et al. Perinatal and obstetric outcomes of donor insemination using cryopreserved semen in Victoria, Australia. Hum Reprod 1999;14:1760-4.
40. Adams DH, Clark RA, Davies MJ, et al. Update on: a meta-analysis of sperm donation offspring health outcomes - 2018 update. J Dev Orig Health Dis 2018;9:561-2.
41. Gaudoin M, Dobbie R, Finlayson A, et al. Ovulation induction/intrauterine insemination in infertile couples is associated with low-birth-weight infants. Am J Obstet Gynecol 2003;188:611-6.
42. Varma TR, Patel RH. Outcome of pregnancy following investigation and treatment of infertility. Int J Gynaecol Obstet 1987;25:113-20.
43. Laivuori HM, Hovatta OLL, Ylikorkala RO. Lack of previous exposure to paternal antigens does not predispose to hypertensive pregnancy complications. Hypertens Preg 1998;17:291-5.
44. Hansen M, Kurinczuk JJ, Bower C, et al. The risk of major birth defects after intracytoplasmic sperm injection and in vitro fertilization. N Engl J Med 2002;346:725-30.
45. Källén B, Finnström O, Nygren KG, et al. In vitro fertilization (IVF) in Sweden: risk for congenital malformations after different IVF methods. Birth Defects Res A Clin Mol Teratol 2005;73:162-9.
46. Bonduelle M, Liebaers I, Deketelaere V, et al. Neonatal

data on a cohort of 2889 infants born after ICSI (1991-1999) and of 2995 infants born after IVF (1983-1999). Hum Reprod 2002;17:671-94.
47. Zhang A, Ma X, Zhang L, et al. Pregnancy and offspring outcomes after artificial insemination with donor sperm: A retrospective analysis of 1805 treatment cycles performed in Northwest China. Medicine (Baltimore) 2019;98:e14975.
48. van der Linde D, Konings EE, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol 2011;58:2241-7.

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