A comparison of pregnancy outcomes and congenital malformations in offspring between patients undergoing intracytoplasmic sperm injection and conventional in vitro fertilization: a retrospective cohort study

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Objective: To explore whether intracytoplasmic sperm injection (ICSI) would increase the malformation risk in fetuses and live births compared with conventional in vitro fertilization (IVF).
Design: Retrospective cohort study.
Patient(s): Data were collected from couples who underwent conventional IVF or ICSI from January 2009 to December 2019 at the Center for Reproductive Medicine of Peking University Third Hospital in the People's Republic of China. A total of 46,167 conventional IVF fresh transfer cycles and 33,247 ICSI fresh transfer cycles were included.
Intervention(s): Intracytoplasmic sperm injection and conventional IVF.
Main Outcome Measure(s): The primary outcomes were congenital abnormalities in live births. The secondary outcomes included the pregnancy outcomes, the malformations among the miscarriages, specific types of malformations in live births, birth weight, and sex.
Result(s): The rates of congenital malformations in conventional IVF and ICSI were 5.44‰ and 5.78‰, respectively. There was no statistically significant difference between the two groups, as indicated by the adjusted odds ratio of 1.098 (95% confidence interval 0.787, 1.532). The rates of specific malformations were comparable between ICSI and IVF. Additionally, no discernible disparities were noted in pregnancy outcomes, the malformations among the miscarriages,birth weight between the two groups.
Conclusion: Our study suggested the safety of ICSI and provided novel evidence by comparing pregnancy outcomes and congenital malformations in offspring between patients undergoing conventional IVF and ICSI. (Fertil Steril® 2024;121:982–90. ©2024 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Reproductive techniques, assisted, sperm injections, intracytoplasmic

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Intracytoplasmic sperm injection (ICSI), which was introduced in 1992, is currently one of the main techniques in assisted reproductive technology (ART) (1). Compared with conventional in vitro fertilization (IVF)-embryo transfer, ICSI can achieve a higher fertilization rate in patients with male infertility (2) by directly injecting one sperm into one oocyte through a microscopy system. It has been reported that ICSI is an appropriate choice in couples with normal sperm who have previously experienced total fertilization failure or a low fertilization rate (<25%) after conventional IVF (3).

Currently, an increasing number of infertile couples without severe male factor are also using ICSI. The International Committee for Monitoring ART reported that ICSI cycles accounted for > 60% of fresh ART cycles in 2014 around the world (4). However, unlike conventional IVF, ICSI is an invasive procedure, and its safety has attracted attention. Whether ICSI is safe is currently debated. It has been reported that offspring conceived by ICSI have an increased risk of congenital malformations (5, 6), epigenetic abnormalities (7, 8), and growth and development problems (including lower Bayley mental development index scores, adiposity, and prelinguistic behavior problems) (9–11). Other studies have shown that ICSI is as safe as conventional IVF in terms of congenital malformations (12, 13), chromosome abnormalities (14), and health outcomes in offspring beyond the neonatal period (including neurodevelopment, growth, vision, and hearing) (15).

There is no doubt that miscarriage, congenital malformations in newborns, and other serious problems can be psychologically and financially devastating to patients. It is necessary to assess the safety of ICSI based on larger-scale data and rigorous data processing measures.

Therefore, we conducted a single-center retrospective cohort study, which included approximately 80,000 cycles, to assess the safety of ICSI by comparing pregnancy outcomes and newborn outcomes with those of conventional IVF based on one of the largest reproductive health centers in the People's Republic of China. The main aim of our study was to explore whether ICSI increases the malformation risk in fetuses and live-born infants, which is meaningful in clinical practice.

MATERIALS AND METHODS

Subjects

This was a retrospective, single-center cohort study involving couples who underwent conventional IVF and ICSI from January 2009 to December 2019 at the Center for Reproductive Medicine of Peking University Third Hospital in the People's Republic of China. Fresh transfer cycles were included, and cycles with insufficient information on basic characteristics were excluded. Ultimately, a total of 46,167 conventional IVF transfer cycles and 33,247 ICSI transfer cycles were included. Among all the fresh transfer cycles, there were 18,749 newborns in conventional IVF group and 13,489 newborns in ICSI group. All patients were followed up by telephone regarding outcomes, and informed consent was obtained from all patients involved in the study.

Data Collection

We collected cycle information, including characteristics of the couples (female age, male age, infertility duration, female body mass index [BMI], basal follicle-stimulating hormone [FSH] levels, basal estradiol [E2] levels, and infertility type), pregnancy outcomes (human chorionic gonadotropin [hCG] positivity, clinical pregnancy, multifetal pregnancy reduction, gestational diabetes mellitus, hypertensive disorders in pregnancy, placenta previa, cesarean section, live birth, monozygotic twinning, miscarriage, and malformations among the miscarriages) and newborn outcomes (gestational age, birth weight, birth length, sex, congenital abnormalities and specific classification).

Congenital abnormalities were classified into congenital malformations of the nervous system (Q00-Q07), congenital malformations of eye, ear, face and neck (Q10-Q18), congenital malformations of the circulatory system (Q20-Q28), congenital malformations of the respiratory system (Q30-Q34), cleft lip and cleft palate (Q35-Q37), congenital malformations of the digestive system (Q38-Q45), congenital malformations of the genital organs (Q50-Q56), congenital malformations of the urinary system (Q60-Q64), congenital malformations and deformations of the musculoskeletal system (Q65-Q79), and chromosomal abnormalities (Q90-Q99) and other congenital malformations (Q80-Q89) based on the "International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)" (16).

All data on patient characteristics and newborn outcomes were obtained from electronic medical records, which were recorded and regularly quality controlled by a dedicated team.

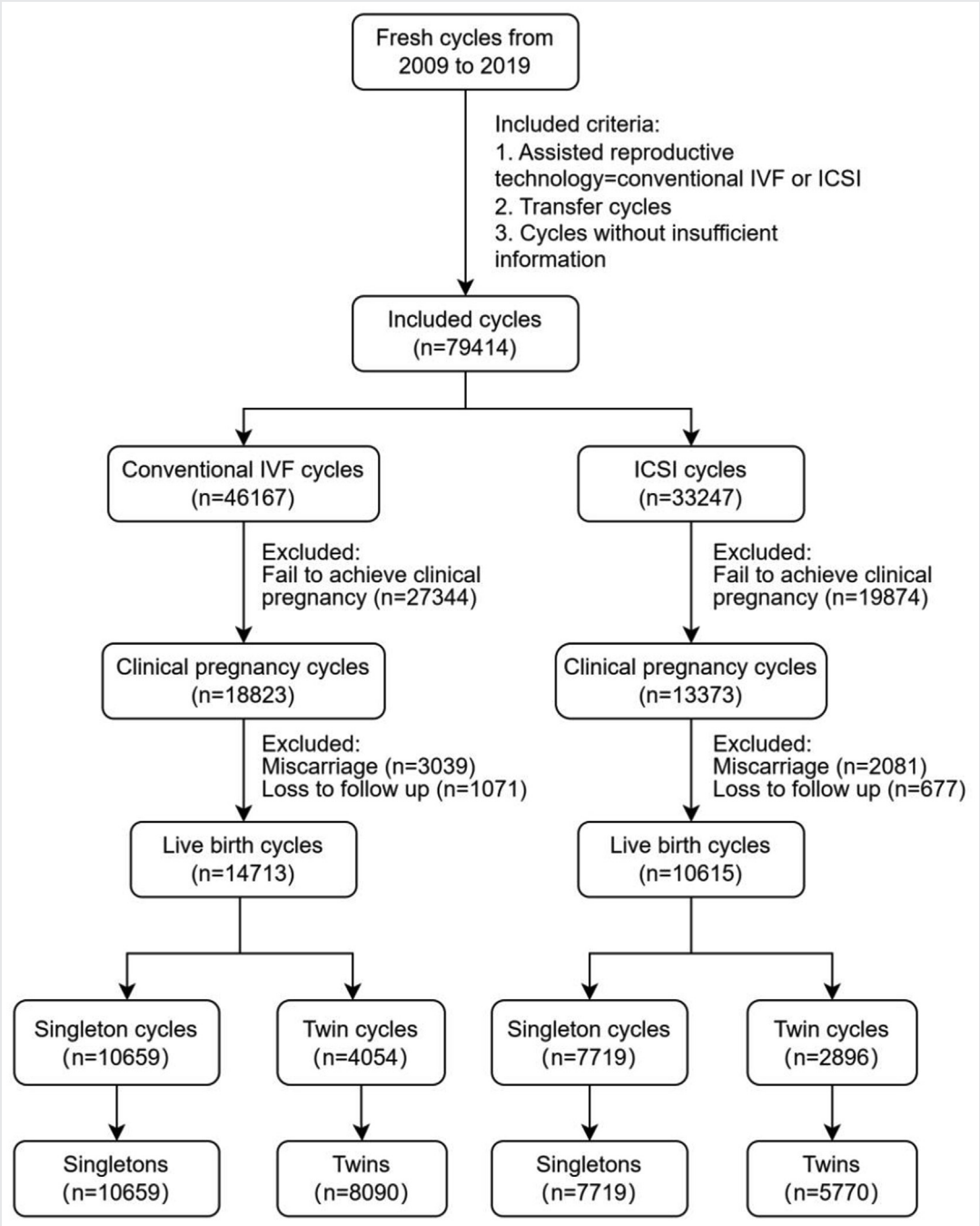
Outcomes

The study outcomes were defined as follows. The hCG positivity rate was calculated as the number of cycles testing positive for hCG/the number of transfer cycles. Clinical pregnancy was diagnosed by ultrasonography, and the clinical pregnancy rate was calculated as the number of clinical pregnancy cycles/the number of transfer cycles (17). The live birth rate was defined as the number of deliveries that resulted in at least one live-born baby/the number of transfer cycles (18). Gestational diabetes mellitus traditionally refers to abnormal glucose tolerance with onset or first recognition during pregnancy (19). Hypertensive disorders in pregnancy are a heterogeneous group of conditions, including chronic hypertension, gestational hypertension, preeclampsia, and preeclampsia superimposed on chronic hypertension (20). The miscarriage rate was defined as the number of pregnancy losses before 28 weeks of gestation/the number of clinical pregnancy cycles. Placenta previa was defined as the placenta covering the cervical os by ultrasonography (21).

Statistical Analysis

Continuous variables were presented as mean ± standard deviation (SD) and compared between groups using the independent samples t-test. Categorical variables were described with the number of cases and percentages (n [%]), and

FIGURE 1



Flowchart of our study.

Zhang. Birth defects of ICSI. Fertil Steril 2024.

comparisons were made using the Chi-squared or Fisher's exact test, as appropriate. Crude odds ratios (ORs) and their 95% confidence intervals (CIs) 95% were calculated to assess the unadjusted effects of fertilization method (ICSI vs. conventional IVF) on congenital malformations and specific types of malformations using logistic regression model.

Additionally, generalized estimating equation (GEE) models were employed to account for the clustering effect of two live births in one pregnancy and repeated pregnancies from the same women. In the GEE model, confounding factors, including female age, male age, infertility duration, female BMI, basal FSH levels, basal E2 levels, infertility type, and pregnancy type, were adjusted. The sensitivity

analysis was conducted to address the potential collider bias made by pregnancy type. All statistical tests were two-sided, and a P value of $<.05$ was considered statistically significant. All statistical analyses were performed using SPSS Statistics, Version 26.0 (IBM Corp., Armonk, New York).

Ethics Statement

The present study protocol was reviewed and approved by the Ethics Committee of Peking University Third Hospital (Reg. no. IRB00006761-M2020007). Informed consent was submitted by all patients at the time of enrollment.

RESULTS

In our retrospective cohort study, a total of 46,167 conventional IVF transfer cycles and 33,247 ICSI transfer cycles were included. A total of 18,823 conventional IVF cycles and 13,373 ICSI cycles resulted in clinical pregnancy. A total of 14,713 conventional IVF cycles and 10,615 ICSI cycles resulted in live-born infants. A total of 18,749 newborns conceived through conventional IVF and 13,489 newborns conceived through ICSI were evaluated (Fig. 1). The comparison between regular follow-up patients and lost patients in clinical pregnancy cycles was conducted (Supplemental Table 1).

Characteristics of Participants

The characteristics of participants were compared in live birth cycles. Compared with the participants who underwent conventional IVF, the participants receiving ICSI treatment had younger female age (31.22 vs. 32.09 years), younger male age (33.09 vs. 33.57 years), longer infertility duration (4.43 vs. 4.18 years), and were more likely to have primary infertility (70.86% vs. 47.33%) (Table 1).

Comparison of Congenital Abnormalities in Live Births

Live-born infants conceived by conventional IVF and ICSI had comparable risks of congenital abnormalities (5.44‰ vs. 5.78‰) and specific types of malformations. The fertilization method had no effect on the congenital abnormality, with an adjusted OR of 1.098 (0.787–1.532) and eleven specific types of malformations (Table 2). We conducted sensitivity analysis and found that excluding the pregnancy type as a parameter had no effect on the above results (Supplemental Table 2, available online).

The pregnancy outcomes of the newborns with congenital malformations between the ICSI and IVF groups were compared. As Table 3 depicts, the rates of gestational diabetes mellitus (2.94% vs. 1.28%), hypertensive disorders in pregnancy (0.98% vs. 1.28%), cesarean section (85.29% vs. 91.03%), as well as the proportion of preterm birth (39.22% vs. 46.15), and birth weight (2,650.81 g vs. 2,626.45 g) were comparable between the two groups (Table 3).

Congenital malformations were compared between conventional IVF and ICSI groups in singletons and twins separately. The rate of congenital malformations in offspring was 4.60‰ in singletons conceived by conventional IVF and 4.15‰ in those conceived by ICSI and increased to 6.55‰ in twins conceived by conventional IVF and 7.97‰ in those conceived by ICSI. No difference was found in the risks of congenital abnormalities and specific types of malformations between conventional IVF and ICSI in singletons (4.60‰ vs. 4.15‰, $P = .648$) or twins (6.55‰ vs. 7.97‰, $P = .327$) (Supplemental Table 3).

The specific congenital malformations in newborns conceived by conventional IVF and ICSI were listed according to ICD-10 codes in the form of eleven classifications (Supplemental Table 4).

Comparison of Pregnancy and Newborn Outcomes

In transfer cycles, the hCG positivity rate (46.10% vs. 45.65%, $P = .209$), clinical pregnancy rate (40.80% vs. 40.22%, $P = .120$), and live birth rate (31.87% vs. 31.93%, $P = .861$) were comparable between the conventional IVF group and ICSI group. In clinical pregnancy cycles, the rates of multifetal

TABLE 1

Basic characteristics of the participants in live birth cycles.

Variables		Conventional IVF (n = 14,713)	ICSI (n = 10,615)	*P* value
Female age (y)		32.09 ± 4.02	31.22 ± 4.22	<.001
Male age (y)		33.57 ± 4.95	33.09 ± 5.41	<.001
Infertility duration (y)		4.18 ± 3.17	4.43 ± 3.22	<.001
Female BMI (kg/m^2)		22.52 ± 3.33	22.46 ± 3.32	.176
Basal FSH (mIU/mL)		6.57 ± 3.17	6.49 ± 3.16	.061
Basal E2 (pmol/L)		151.43 ± 71.71	149.80 ± 68.05	.066
Infertility type (%)	Primary	6,963 (47.33)	7,522 (70.86)	<.001
	Secondary	7,750 (52.67)	3,093 (29.14)	
Pregnancy type (%)	Singletons	10,659 (72.45)	7,719 (72.72)	.633
	Twins	4,054 (27.55)	2,896 (27.28)	

Note: Values are presented as the mean ± SD or the n (%). BMI = body mass index; E2 = estradiol; FSH = follicle-stimulating hormone; SD = standard deviation.

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TABLE 2

Comparison of congenital abnormalities among live births.

Variables	Conventional IVF (n = 18,749)	ICSI (n = 13,489)	ICSI vs. conventional IVF: Unadjusted OR (95% CI) *P* value	ICSI vs. conventional IVF: Adjusted OR (95% CI)[a] *P* value
Congenital abnormality (‰)	102 (5.44)	78 (5.78)	1.063 (0.791–1.429) .684	1.098 (0.787–1.532) .581
Nervous system (‰)	9 (0.48)	8 (0.59)	1.236 (0.477–3.203) .663	1.259 (0.380–4.177) .706
Eye, ear, face, and neck (‰)	12 (0.64)	7 (0.52)	0.811 (0.319–2.060) .659	0.737 (0.254–2.139) .575
Circulatory system (‰)	26 (1.39)	25 (1.85)	1.337 (0.772–2.316) .300	1.368 (0.735–2.546) .322
Respiratory system (‰)	5 (0.27)	9 (0.67)	2.503 (0.839–7.470) .100	2.059 (0.601–7.048) .250
Cleft lip and cleft palate (‰)	8 (0.43)	7 (0.52)	1.216 (0.441–3.355) .705	1.087 (0.358–3.305) .883
Digestive system (‰)	8 (0.43)	6 (0.44)	1.042 (0.362–3.005) .939	1.227 (0.406–3.710) .716
Genital organs (‰)	5 (0.27)	2 (0.15)	0.556 (0.108–2.866) .483	0.609 (0.102–3.648) .587
Urinary system (‰)	8 (0.43)	3 (0.22)	0.521 (0.138–1.965) .336	0.501 (0.121–2.069) .339
Musculoskeletal system (‰)	18 (0.96)	12 (0.89)	0.927 (0.446–1.924) .838	1.192 (0.547–2.599) .658
Chromosomal abnormalities (‰)	4 (0.21)	2 (0.15)	0.695 (0.127–3.795) .695	0.808 (0.192–3.392) .771
Other congenital malformations (Congenital malformations of adrenal gland, ‰)	1 (0.05)	0 (0.00)	—	—

Note: Values are presented as the n (‰) or the odds ratio (95% confidence interval). CI = confidence interval; ICSI = intracytoplasmic sperm injection; IVF = in vitro fertilization; OR = odds ratio. One patient with multiple malformations was counted once in congenital abnormality but included in more than one specific system of malformation.

[a] Adjusted by female age (y), male age (y), infertility duration (y), female body mass index (kg/m^2), follicle-stimulating hormone (mIU/mL), estradiol (pmol/L), infertility type and pregnancy type.

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pregnancy reduction (1.55% vs. 1.41%, $P = .314$), gestational diabetes mellitus (0.49% vs. 0.36%, $P = .070$), hypertensive disorders in pregnancy (0.78% vs. 0.72%, $P = .554$), placenta previa (0.36% vs. 0.37%, $P = .792$), cesarean section (61.81% vs. 62.47%, $P = .232$) and monozygotic twinning (0.80% vs. 0.64%, $P = 0.084$) were comparable between the conventional IVF group and ICSI group (Supplemental Table 5).

In clinical pregnancy cycles, there was no significant difference in the miscarriages (16.15% vs. 15.56%, $P = .158$), the malformations among the miscarriages (4.94‰ vs. 5.16‰, $P = .784$), or the eleven specific malformations (including malformations of the nervous system, malformations of the head and neck, malformations of the circulatory system, malformations of the respiratory system, cleft lip and cleft palate, malformations of the digestive system, malformations of genital organs, malformations of the urinary system, malformations of the musculoskeletal system and chromosomal abnormalities) among the miscarriages between the conventional IVF group and ICSI group (Supplemental Table 6).

TABLE 3

Comparison among live births with congenital malformations.

Variables		Conventional IVF (n = 102)	ICSI (n = 78)	*P* value
Gestational diabetes mellitus (%)		3 (2.94)	1 (1.28)	.812
Hypertensive disorders in pregnancy (%)		1 (0.98)	1 (1.28)	>.999
Cesarean section (%)		87 (85.29)	71 (91.03)	.245
Gestational age (%)	Preterm birth	40 (39.22)	36 (46.15)	.339
	<32 wk	12 (11.76)	8 (10.26)	.755
	32–36 wk	28 (27.45)	28 (35.90)	.219
Birth weight (g)		2,650.81 ± 806.95	2,626.45 ± 785.02	.845
Sex (%)	Male	66 (64.71)	43 (55.13)	.193
	Female	36 (35.29)	35 (44.87)	

Note: Values are presented as the mean ± SD or the n (%). IVF = in vitro fertilization.

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The proportion of preterm birth in ICSI group was lower than that in conventional IVF group (20.72% vs. 22.64%, $P < .001$). The proportion of preterm birth (32–36 weeks) was lower in ICSI patients than in conventional IVF patients (18.49% vs. 20.41%, $P < .001$), while the proportion of preterm birth (< 32 weeks) was comparable between the two groups. No difference was found in the birth weight (2,977.41 g vs. 2,988.28 g) between the conventional IVF group and ICSI group. Secondary sex ratio (Number of male babies/Number of total babies) after ICSI was lower than that after conventional IVF (49.51% vs. 53.66%, $P < .001$) (Supplemental Table 5).

DISCUSSION

We conducted a single-center retrospective cohort study to assess the safety of ICSI by comparing pregnancy outcomes and newborn outcomes between a conventional IVF group and an ICSI group. Our study showed that the conventional IVF group and the ICSI group had comparable pregnancy outcomes and congenital abnormality rates.

There were significant differences in basic characteristics between the conventional IVF group and the ICSI group, which might be due to our large sample size and the different indications for the two fertilization methods (22).

The effect of ICSI on congenital malformations in offspring remains controversial. A review showed no difference between newborns conceived by conventional IVF and ICSI in terms of the risks of overall congenital malformations (12). One cohort study on the risk of birth defects among infants after conventional IVF and ICSI showed that the risks of congenital malformations and specific malformations after ICSI were comparable with those after conventional IVF (23). A meta-analysis showed that the risks of genitourinary malformations in offspring conceived in conventional IVF and ICSI cycles were comparable by including four studies with a low risk of bias (24). However, one cohort study in Australia drew an inconsistent conclusion. In this study, the unadjusted prevalence rate of congenital abnormalities was 7.1% in the conventional IVF group and 9.9% in the ICSI group, and the rate of congenital abnormalities in the ICSI group was higher with regard to nulliparity and lower among smokers than that in the conventional IVF group (5). In our study, newborns conceived by conventional IVF and ICSI had comparable risks of congenital abnormalities and specific types of malformations.

The ICSI performed well in pregnancy outcomes. It was reported that the rates of clinical pregnancy, live births, gestational diabetes mellitus, hypertensive disorders in pregnancy, placenta previa, cesarean section, and miscarriage were comparable between the conventional IVF group and the ICSI group (25–27). Previous studies showed that there was no significant difference in the incidence of embryonic anomalies leading to abortion between the conventional IVF and ICSI groups (28, 29). We found no significant difference in pregnancy outcomes or malformations leading to abortions between the conventional IVF group and the ICSI group, which was in accordance with previous studies.

In ICSI treatment, ovarian stimulation, in vitro culture conditions, and specific alterations of the zona pellucida might increase the monozygotic twinning rate (30). It was reported that compared with natural conception, ICSI led to a higher risk of monozygotic twinning (31). The mechanism of this phenomenon is still unclear. However, previous studies showed that ICSI had a comparable monozygotic twinning rate with conventional IVF and suggested that ICSI should not be recognized as a risk factor (32, 33). Our study had a large sample size and showed that the monozygotic twinning rate of ICSI was not higher than that of conventional IVF.

Previous studies suggested that ICSI was less likely to cause preterm birth than conventional IVF (27, 34, 35). A population-based cohort study proposed that the phenomenon could be attributed to infertility factors (36). Our study showed that the incidence of preterm birth (32–36 weeks) was lower in ICSI patients than in conventional IVF patients. Patients receiving ICSI treatment tended to be younger, and the indications for ICSI and IVF were different, so the difference in gestational age needs to be further studied. In our study, secondary sex ratio after ICSI was lower than that after conventional IVF. Several studies reported that ICSI decreased the percentage of male offspring, which was in accordance with our results (37, 38).

Our study had several strengths. First, we screened 46,167 conventional IVF transfer cycles and 33,247 ICSI transfer cycles from January 2009 to December 2019. Our study was based on a large sample size. Second, the follow-up rate of patients was high, and the follow-up procedure was standardized in our study. Therefore, the findings of our study are credible and can better guide clinical work. Third, our study obtained data from electronic medical records, which were credible and could avoid recall bias. Moreover, our study provided novel evidence by reporting a comprehensive comparison of malformations between patients undergoing conventional IVF and ICSI.

Our study has some limitations that need to be addressed. First, the etiology of miscarriage was poorly tracked, potentially impacting the accuracy of comparing malformations between conventional IVF and ICSI groups among miscarriages. Second, as our study is based on a single-center cohort in China, the generalizability of the findings to other populations requires further validation. Third, we included all fresh transfer cycles but compared the primary outcome (congenital abnormality) in the live births, which might introduce collider bias. Moreover, despite encompassing all live birth fresh IVF and ICSI cycles from 2009 to 2019 in our center, the limited number of positive events (congenital malformations) resulted in a relatively wide CI range for the OR assessing the effect of ICSI versus conventional IVF on the presence of congenital abnormalities. This wide range requires careful consideration when attempting to conclusively interpret the absence of an effect, introducing uncertainty that cannot be fully excluded from the results.

CONCLUSION

We performed a large single-center retrospective cohort study to assess the safety of ICSI by comparing the pregnancy outcomes and newborn outcomes with those of ICSI. Our study showed that ICSI performed as well as conventional IVF in terms of pregnancy and newborn outcomes. The incidence of congenital malformations in offspring was comparable between conventional IVF group and ICSI group.

CRediT Authorship Contribution Statement

Nan Zhang: Writing – original draft, Formal analysis, Data curation, Conceptualization. **Tian Tian:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Jia Li:** Writing – review & editing, Supervision. **Xiaxuan Zhu:** Conceptualization. **Dina Jiesisibieke:** Conceptualization. **Shilin Fang:** Conceptualization. **Ping Liu:** Writing – review & editing, Supervision. **Rong Li:** Writing – review & editing, Supervision. **Jie Qiao:** Writing – review & editing, Supervision. **Rui Yang:** Writing – review & editing, Supervision, Funding acquisition.

Declaration of interests

N.Z. has nothing to disclose. T.T. has nothing to disclose. J.L. has nothing to disclose. X.Z. has nothing to disclose. D.J. has nothing to disclose. S.F. has nothing to disclose. P.L. has nothing to disclose. R.L. has nothing to disclose. J.Q. has nothing to disclose. R.Y. has nothing to disclose.

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Comparación de los resultados del embarazo y las malformaciones congénitas en la descendencia entre pacientes sometidos a inyección intracitoplasmática de espermatozoides y fecundación in vitro convencional: un estudio de cohorte retrospectivo.

Objetivo: Explorar si la inyección intracitoplasmática de espermatozoides (ICSI) aumentaría el riesgo de malformaciones en fetos y nacidos vivos en comparación con la fecundación in vitro (FIV) convencional.

Diseño: Estudio de cohorte retrospectivo.

Paciente(s): Los datos se recopilaron en parejas que se sometieron a FIV o ICSI convencional desde enero de 2009 hasta diciembre de 2019 en el Centro de Medicina Reproductiva del Tercer Hospital de la Universidad de Pekín en la República Popular China. Se incluyeron un total de 46.167 ciclos de transferencia en fresco de FIV convencional y 33.247 ciclos de transferencia en fresco de ICSI.

Intervención(es): Inyección intracitoplasmática de espermatozoides y FIV convencional.

Principales medidas de resultado: Los resultados primarios fueron anomalías congénitas en los nacidos vivos. Los resultados secundarios incluyeron los resultados del embarazo, las malformaciones entre los abortos espontáneos, tipos específicos de malformaciones en los nacidos vivos, el peso al nacer y el sexo.

Resultado(s): Las tasas de malformaciones congénitas en FIV e ICSI convencionales fueron de 5,44% y 5,78%, respectivamente. No hubo diferencias estadísticamente significativas entre los dos grupos, como lo indica el odds ratio ajustado de 1,098 (intervalo de confianza del 95%: 0,787; 1,532). Las tasas de malformaciones específicas fueron comparables entre ICSI y FIV. Además, no se observaron disparidades discernibles en los resultados del embarazo, las malformaciones entre los abortos espontáneos y el peso al nacer entre los dos grupos.

Conclusión: Nuestro estudio sugirió la seguridad de la ICSI y proporcionó evidencia novedosa al comparar los resultados del embarazo y las malformaciones congénitas en la descendencia entre pacientes sometidas a FIV convencional e ICSI.