Previous Cesarean Delivery Affect Pregnancy Outcomes After *in Vitro* Fertilization and Frozen-thawed Embryo Transfer: a Retrospective Cohort Study

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Research Article

Keywords: Cesarean delivery history, Cesarean scar defect, IVF, frozen-thawed embryo transfer, live birth

Posted Date: February 16th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1339106/v1

Abstract

Background: To investigate the impact of previous cesarean delivery (CD) on pregnancy outcomes after *in vitro* fertilization (IVF) and frozen-thawed embryo transfer (FET).

Methods: We conducted a retrospective cohort study that included 1122 women aged <40 years who had a history of only one parturition (after 28 weeks of pregnancy) and were undergoing their first FET cycle between January 2014 and January 2020. Live birth, clinical pregnancy, multiple pregnancy, ectopic pregnancy, pregnancy loss, pregnancy complications, preterm birth, and neonatal birth weight were compared among patients treated with IVF and FET. Multivariate logistic regression was performed to evaluate the relationship between pregnancy outcomes and FET.

Results: After adjustment for confounders, in the single embryo transfer (SET) patients, the adjusted OR for a subsequent live birth was 0.75(95% CI: 0.39–1.42, P=0.370) in women with previous CD and 0.48 (95% CI: 0.18–1.27, P=0.140) in women with a cesarean scar defect (CSD), compared to women with previous vaginal delivery (VD). In the double embryo transfer (DET) patients, the adjusted OR for a subsequent live birth was 0.57(95% CI: 0.41–0.81, P=0.001) in women with previous CD and 0.37(95% CI: 0.20–0.70, P=0.002) in women with a CSD, compared to women with previous VD.

Conclusions: Previous CD and the presence of a CSD reduced the success of clinical pregnancy and live birth among patients who received IVF-FET treatment, especially in DET patients.

Introduction

Cesarean delivery (CD) is a method to solve problems associated with obstetric complications, which can reduce mortality rates among mothers and newborns. With the development of perinatal medicine, including improvements in anesthesia and CD technology and the use of antibiotics, the safety of CD has been widely recognized by society. Proper use of CD plays an important role in reducing maternal and perinatal infant mortality and morbidity [1-3]. However, due to various iatrogenic and social factors, the global CD rate has risen sharply in the past 30 years [4,5]. For example, in 1979, China enacted the one-child policy so most couples could only have one child, leading to a dramatic rise in CDs without obstetric indications [6,7]. During the 20 years from 1988 to 2008, the CD rate in China rose from 3.4% to 39.3% [8]. Since 2013, the two-child policy has been gradually rolled out in order to help to deal with the aging population. A study [9] showed that the overall hospital CD rate decreased from 45.3% in 2012 to 41.1% in 2016 after the one-child policy was relaxed. Despite this decline, the proportion of pregnant women with previous CD nearly doubled, from 9.8% to 17.7%. It is more complicated and dangerous for women with a scarred uterus to undergo pregnancy again compared to women with previous vaginal delivery (VD) [10]. In addition, CD is associated with many complications, including cesarean scar defect (CSD), which is also known as isthmocele, uterine transmural hernia, diverticulum, pouch, and niche [11]. CSD is characterized by defective myometrium healing at the site of the cesarean incision and commonly causes postmenstrual spotting, dysmenorrhea, chronic pelvic pain, dyspareunia, and infertility [12,13].

The CSD prevalence ranges from 6.9% to 69% of the women who had undergone one CD [14]. Hysterosalpingography, transvaginal sonography (TVS), saline infusion sonohysterography, hysteroscopy, and magnetic resonance imaging can be used to diagnose CSD [15]. However, the current literature lacks data on the associations between CSD and pregnancy outcomes after *in vitro* fertilization (IVF)-embryo transfer (ET).

This study used a retrospective cohort design to analyze the associations of previous CD and CSD with the pregnancy outcomes of patients undergoing frozen-thawed embryo transfer (FET).

Methods

Study design and population

We conducted a retrospective cohort study of patients who received an FET cycle at the Tianjin Central Hospital of Gynecology Obstetrics from January 2014 to January 2020. The study design is shown in Fig.1. The inclusion criteria were as follows: received their first FET cycle, had a history of only one parturition (after 28 weeks of pregnancy), and were aged <40 years. The exclusion criteria were as follows: congenital uterine malformation, either or both spouses had chromosome abnormalities, diabetes or hypertension, oligomenorrhea or polycystic ovary syndrome (PCOS), endometriosis or adenomyosis, and missing clinical data.

All patients underwent TVS at least two times during the treatment. If TVS shows a pouch-like anechoic area with a depth ≥2 mm at the cesarean incision, the patient can be diagnosed with CSD [16,17]. We also used TVS to measure the size of the CSD.

Patients meeting the inclusion and exclusion criteria were divided into the following groups: CD group (group A), VD group (group B), and CSD group (group C). Thereafter, according to the number of transferred embryos, groups A, B, and C were respectively divided into single embryo transfer (SET) groups (A1, B1, and C1) and double embryo transfer (DET) groups (A2, B2, and C2).

Endometrial preparation and embryo transfer

Based on each patient's menstruation and clinical condition, a modified natural cycle or a hormone replacement therapy cycle was selected to prepare the endometrium. All frozen embryos underwent routine vitrification and thawing. The embryos in the cleavage stage were thawed and transferred on the third day after ovulation; the blastocysts were thawed and transferred on the fifth day after ovulation. Up to two embryos were transferred per cycle. Luteal support and oral dydrogesterone were prescribed for all patients after ET. TVS was performed 28 days after ET to confirm the pregnancy.

Variables

We collected the patients' basic information, including age, body mass index (BMI), infertility duration, infertility factors, endometrial preparation, basal follicle-stimulating hormone (FSH), basal luteinizing

hormone (LH), basal estradiol (E2), number of retrieved oocytes, and high-quality embryo rate. The primary outcome was live birth. The secondary outcomes were clinical pregnancy, multiple pregnancy, ectopic pregnancy, pregnancy loss, pregnancy complications, preterm birth, and neonatal birth weight (low, high, and normal birth weight).

Statistical analysis

The continuous variables are expressed as mean and standard deviation ($\bar{x}$±SD). The Mann–Whitney U test was used to compare continuous variables that were non-normally distributed. The primary and secondary outcomes are expressed as frequency (percentage) and compared using Pearson's χ^2 test or Fisher's exact test. Multivariate-adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were calculated using logistic regression models. The covariates were age, pre-pregnancy BMI, infertility duration, infertility diagnosis, endometrial preparation, basal FSH, basal LH, basal E2, number of oocytes retrieved, and high-quality embryo rate. $P<0.05$ was considered to indicate statistically significant differences. All statistical procedures were conducted in SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 1122 patients were retrospectively enrolled in the study. We followed up one year and obtained information on the clinical pregnancy outcomes of them. 129 patients (15.6%) were diagnosed with CSD (mean length: 0.42±0.21 cm, mean width: 0.38±0.17 cm, and mean depth: 0.70±0.14 cm). Among the 409 patients who underwent SET, 300 had previous CD, 54 had previous VD, and 55 had a CSD. Their demographics and cycle characteristics are presented in Table 1. There were no significant differences in these variables between the three SET groups, except for age between groups A1 and C1. Among the remaining 713 patients who underwent DET, 400 had previous CD, 239 had previous VD, and 74 had a CSD. Their demographics and cycle characteristics are presented in Table 2. The three DET groups exhibited significant differences in age, infertility duration, and basal FSH.

Table 1 Demographics and cycle characteristics in single embryo transfer (SET) groups (n=409)

				P			
	A1 （n=300）	B1（n=54）	C1（n=55）	A1&B1	A1&C1	B1&C1	T *P*
Age (years)	33.5±3.7	33.8±3.9	34.9±4.7	0.591[1]	0.015[1]	0.190[1]	0.051[1]
Body Mass Index (kg/m2)	23.4±3.2	23.2±2.9	23.6±3.0	0.630[1]	0.732[1]	0.505[1]	0.813[1]
Duration of infertility (years)	4.2±3.1	5.1±3.2	4.4±3.2	0.072[1]	0.746[1]	0.272[1]	0.200[1]
Infertility diagnosis,n(%)				0.745[2]	0.176[2]	0.567[2]	0.461[2]
Male factor	47 (15.7)	9 (16.7)	4 (7.3)				
Tubal factor	118 (39.3)	18 (33.3)	17 (30.9)				
Other	75 (25.0)	12 (22.2)	17 (30.9)				
Unexplained	7 (2.3)	2 (3.7)	2 (3.6)				
Combined	53 (17.7)	13 (24.1)	15 (27.3)				
Endometrial preparation,n(%)				0.992[2]	0.873[2]	0.909[2]	0.987[2]
Modified natural cycle	178 (59.3)	32 (59.3)	32 (58.2)				
HRT	122 (40.7)	22 (40.7)	23 (41.8)				
Basal FSH (mIU/L)	6.4±2.1	6.1±2.4	6.7±1.9	0.379[1]	0.311[1]	0.159[1]	0.350[1]
Basal LH (mIU/L)	4.3±2.7	3.9±2.7	4.0±1.9	0.297[1]	0.437[1]	0.795[1]	0.463[1]
Basal E2 (mIU/L)	44.7±24.3	40.1±16.3	48.4±33.2	0.177[1]	0.330[1]	0.099[1]	0.213[1]
No. oocytes retrieved	17.6±8.5	17.2±8.7	17.5±10.5	0.736[1]	0.950[1]	0.896[1]	0.946[1]
High-quality embryo rate	25.0±42.9	21.3±39.6	26.2±34.7	0.559[1]	0.844[1]	0.499[1]	0.801[1]
Stage of embryo				0.927[2]	0.535[2]	0.576[2]	0.811[2]
Cleavage	246 （82.0）	44（81.5）	47（85.5）				
Blastocyst	54（18.0）	10（18.5）	8（14.5）				

E2: estradiol; FSH: follicle-stimulating hormone; LH: luteinizing hormone; A1: previous cesarean delivery (CD) and single embryo transfer (SET); B1: previous vaginal delivery (VD) and SET; C1: cesarean scar defect (CSD) and SET. Data are mean±SD unless stated otherwise.

[1] One-way analysis of variance. [2] Pearson's $\chi 2$ test.

Table 2 Demographics and cycle characteristics in double embryo transfer (DET) groups (n=713)

				P			
	A2 （n=400）	B2 （n=239）	C2（n=74）	A2&B2	A2&C2	B2&C2	T *P*
Age (years)	33.7±3.4	34.3±3.5	35.5±5.2	0.031[1]	<0.001[1]	0.024[1]	0.000[1]
Body Mass Index (kg/m2)	23.1±3.1	22.8±2.9	22.5±3.9	0.433[1]	0.191[1]	0.410[1]	0.362[1]
Duration of infertility (years)	4.2±3.1	4.8±3.3	4.5±3.2	0.014[1]	0.386[1]	0.514[1]	0.048[1]
Infertility diagnosis,n(%)				0.075[2]	0.843[2]	0.794[2]	0.320[2]
Male factor	70 (17.5)	38 (15.9)	10 (13.5)				
Tubal factor	137 (34.4)	101 (42.3)	28 (37.8)				
Other	105 (26.3)	55 (23.0)	21 (28.4)				
Unexplained	12 (3.0)	13 (5.4)	3 (4.1)				
Combined	76 (19.8)	32 (13.4)	12 (16.2)				
Endometrial preparation,n(%)				0.851[2]	0.976[2]	0.931[2]	0.982[2]
Modified natural cycle	244 (61.0)	144 (60.3)	45 (60.8)				
HRT	156 (39.0)	95 (39.7)	29 (39.2)				
Basal FSH (mIU/L)	6.5±1.8	6.3±2.1	6.9±2.2	0.112[1]	0.133[1]	0.036[1]	0.053[1]
Basal LH (mIU/L)	4.0±2.2	3.9±1.8	3.5±1.4	0.702[1]	0.089[1]	0.097[1]	0.208[1]
Basal E2 (mIU/L)	43.4±26.2	46.4±20.2	45.4±20.2	0.151[1]	0.532[1]	0.582[1]	0.307[1]
No. oocytes retrieved	16.9±7.3	16.9±7.4	15.0±6.1	0.920[1]	0.104[1]	0.099[1]	0.244[1]
High-quality embryo rate	26.0±37.3	32.4±41.7	33.7±29.1	0.051[1]	0.108[1]	0.813[1]	0.077[1]
Stage of embryo				0.374[2]	0.437[2]	0,871[2]	0.583[2]
Cleavage	377 （94.3）	221 （92.5）	68（91.9）				
Blastocyst	23（5.8）	18（7.5）	6（8.1）				

E2: estradiol; FSH: follicle-stimulating hormone; LH: luteinizing hormone; A2: previous cesarean delivery (CD) and double embryo transfer (DET); B2: previous vaginal delivery (VD) and DET; C2: cesarean scar defect and DET.

[1] One-way analysis of variance. [2] Pearson's χ^2 test.

The results of the unadjusted analyses are shown in Tables 3 and 4. In SET patients (Table 3), the clinical pregnancy and live birth rates decreased in C1 (27.3% and 23.6%, respectively) compared to in group B1 (44.4% and 35.2%, respectively) or group A1 (39.0% and 30.3%, respectively), but there were no significant differences in any of the pregnancy outcomes among the three SET groups (P>0.05), except for neonatal birth weight. In contrast, in DET patients (Table 4), the clinical pregnancy and live birth rates were significantly lower in group C2 (33.8% and 24.3%, respectively) compared to in group A2 (46.8% and 36.8%, respectively) or in group B2 (59.8% and 49.4%, respectively), and in group A2 compared to group B2 (P<0.05). Moreover, in DET patients, the multiple pregnancy rate was significantly lower in group A2 (10.8%) and C2 (9.5%) than group B2 (20.1%) (P<0.05 for both). In the DET patients, ectopic pregnancies only occurred in group A2, which had five cases. There were no significant differences in pregnancy loss rate, pregnancy complication rate, preterm birth rate, or neonatal birth weight among the three DET groups (P>0.05).

Table 3 Single embryo transfer (SET) reproductive outcomes (unadjusted analysis)

				P			
	A1 (n=300)	B1 (n=54)	C1 (n=55)	A1 vs. B1	A1 vs. C1	B1 vs. C1	T *P*
Clinical pregnancy, n (%)	117 (39.0)	24 (44.4)	15 (27.3)	0.452[1]	0.098[1]	0.061[1]	0.153[1]
Pregnancy loss, n (%)	22 (18.8)	3 (12.5)	2 (13.3)	0.461[1]	0.605[1]	0.940[1]	0.692[1]
Early pregnancy loss, n (%)	20 (17.1)	3 (12.5)	2 (13.3)	0.579[1]	0.713[1]	0.940[1]	0.818[1]
Late pregnancy loss, n (%)	2 (1.7)	0	0	0.519[1]	0.610[1]	NA	0.713[1]
Ectopic pregnancy, n (%)	3 (2.6)	1 (4.2)	0	0.667[1]	0.530[1]	0.423[1]	0.726[1]
Pregnancy complications, n (%)	18 (15.4)	5 (20.8)	0	0.510[1]	0.102[1]	0.058[1]	0.188[1]
Preterm birth, n (%)	12 (13.2)	4 (21.1)	2 (15.4)	0.376[1]	0.828[1]	0.687[1]	0.675[1]
Live birth, n (%)	91 (30.3)	19 (35.2)	13 (23.6)	0.478[1]	0.316[1]	0.186[1]	0.414[1]
LBW, n (%)	6 (6.6)	0	0	0.250[1]	0.340[1]	NA	0.330[1]
NBW, n (%)	74 (81.3)	12 (63.2)	13 (100)	0.081[1]	0.088[1]	0.013[1]	0.033[1]
HBW, n (%)	11 (12.1)	7 (36.8)	0	0.008[1]	0.185[1]	0.013[1]	0.006[1]

LBW: low birth weight; HBW: high birth weight; NBW: normal birth weight.

[1]Pearson's χ^2 test

Table 4 Double embryo transfer (DET) reproductive outcomes (unadjusted analysis)

				P			
	A2 (n=400)	B2 (n=239)	C2 (n=74)	A2 vs. B2	A2 vs. C2	B2 vs. C2	T *P*
Clinical pregnancy, n (%)	187 (46.8)	143 (59.8)	25 (33.8)	0.001[1]	0.039[1]	<0.001[1]	<0.001[1]
Multiple pregnancy, n (%)	43 (10.8)	48 (20.1)	7 (9.5)	0.001[1]	0.740[1]	0.036[1]	0.002[1]
Pregnancy loss, n (%)	33 (17.6)	24 (16.8)	7 (28.0)	0.837[1]	0.214[1]	0.182[1]	0.396[1]
Early pregnancy loss, n (%)	27 (14.4)	18 (12.6)	6 (24.0)	0.627[1]	0.216[1]	0.132[1]	0.324[1]
Late pregnancy loss, n (%)	6 (3.2)	6 (4.2)	1 (4.0)	0.635[1]	0.835[1]	0.964[1]	0.890[1]
Ectopic pregnancy, n (%)	5 (2.7)	0	0	0.049[1]	0.408[1]	NA	0.102[1]
Pregnancy complications, n (%)	36 (19.3)	21 (14.7)	5 (20.0)	0.277[1]	0.929[1]	0.498[1]	0.524[1]
Preterm birth, n (%)	33 (22.4)	20 (16.9)	6 (33.3)	0.266[1]	0.305[1]	0.100[1]	0.221[1]
Live birth, n (%)	147 (36.8)	118 (49.4)	18 (24.3)	0.002[1]	0.039[1]	<0.001[1]	<0.001[1]
LBW, n (%)	23 (13.5)	26 (17.3)	4 (20.0)	0.346[1]	0.433[1]	0.769[1]	0.551[1]
NBW, n (%)	137 (80.6)	114 (76.0)	15 (75.0)	0.319[1]	0.555[1]	0.922[1]	0.572[1]
HBW, n (%)	10 (5.9)	10 (6.7)	1 (5.0)	0.772[1]	0.873[1]	0.776[1]	0.935[1]

LBW: low birth weight; HBW: high birth weight; NBW: normal birth weight.

[1] Pearson's χ^2 test.

Logistic regression was performed to determine the effects of previous CD and CSD on clinical pregnancy, multiple pregnancy, pregnancy loss, preterm birth, and live birth while adjusting for age, pre-pregnancy BMI, infertility duration, infertility diagnosis, endometrial preparation, basal FSH, basal LH, basal E2, number of oocytes retrieved, and high-quality embryo rate as potential confounders. The results are presented in Tables 5. In SET patients, CSD (compared to previous VD) was associated with a significantly lower clinical pregnancy rate (adjusted OR 0.31, 95% CI: 0. 12–0. 81, P=0.017). In DET patients, previous CD (compared to previous VD) was associated with a significantly lower clinical pregnancy rate (adjusted OR 0. 56, 95% CI: 0. 40–0. 79, P=0.001), multiple pregnancy rate (adjusted OR 0.

42, 95% CI: 0. 26–0. 68, P=0.001), and live birth rate (adjusted OR 0. 57, 95% CI: 0. 41–0. 81, P=0.001). Additionally, in DET patients, CSD (compared to previous VD) was associated with a significantly lower clinical pregnancy rate (adjusted OR 0. 39, 95% CI: 0. 21–0.72, P=0.002) and live birth rate (adjusted OR 0. 37, 95% CI: 0. 20–0. 70, P=0.002). Previous CD and CSD were not significantly associated with pregnancy complications, pregnancy loss, or preterm birth.

Table 5 Multivariate logistic regression analysis for the patients of following frozen embryo transfer.

	A1（n=409）		A2（n=713）		C1（n=409）		C2（n=713）	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Clinical pregnancy	0.74 (0.40-1.36)	0.331	0.56 (0.40-0.79)	0.001	0.31 (0.12-0.81)	0.017	0.39 (0.21-0.72)	0.002
Multiple pregnancy	NA	NA	0.42 (0.26-0.68)	<0.001	NA	NA	0.47 (0.19-1.15)	0.098
Pregnancy loss	1.65 (0.43-6.29)	0.464	1.05 (0.58-1.90)	0.876	0.03 (0.00-15.59)	0.273	1.97 (0.71-5.47)	0.193
Early pregnancy loss	1.46 (0.38-5.58)	0.582	1.15 (0.59-2.24)	0.678	0.03 (0.00-15.59)	0.273	2.22 (0.73-6.74)	0.159
Late pregnancy loss	NA	NA	0.77 (0.24-2.49)	0.658	NA	NA	1.36 (0.14-13.47)	0.793
Pregnancy complications	NA	NA	1.30 (0.70-2.39)	0.407	NA	NA	2.07 (0.63-6.74)	0.228
Live birth	0.75 (0.39-1.42)	0.370	0.57 (0.41-0.81)	0.001	0.48 (0.18-1.27)	0.140	0.37 (0.20-0.70)	0.002
Preterm birth	0.67 (0.17-2.61)	0.559	1.26 (0.67-2.39)	0.476	0.82 (0.04-18.88)	0.900	1.61 (0.42-6.13)	0.484

A1:cesarean delivery of single embryo transfer, A2:cesarean delivery of double embryo transfer, C1:previous cesarean scar defect of single embryo transfer, C2:previous cesarean scar defect of double embryo transfer,PCSD of double embryo transfer.

Discussion

Our study showed that during an FET cycle, previous CD negatively affects pregnancy outcomes after SET or DET. In the unadjusted analyses, the clinical pregnancy and live birth rates were significantly lower in patients with previous CD than in patients with previous VD, but only in the DET patients ($P<0.05$). We then used multivariate logistic regression to adjust for potential confounding factors. The overall results did not change (i.e., among the DET patients, the clinical pregnancy and live birth rates continued to be significantly lower in patients with previous CD than in patients with previous VD), except for the fact that, among the SET patients, the decrease in the clinical pregnancy rate in CSD patients compared to patients with previous VD became significant ($P=0.017$). Several previous studies report similar results to ours. Vissers et al. [18] reported that previous CD reduced the live birth rate after IVF-ET, in both the general population group and the SET subgroup. Marjolein et al. [19] also reported that previous CD was associated with a reduced live birth rate after ET.

There are also several conflicting results. A study by Patounakis et al. [20] found that ETs in patients with previous CD took >30 seconds and the catheters were more likely to be covered in blood or mucus than in the ETs involving patients with previous VD. However, there were no differences in pregnancy outcomes between patients with different delivery histories. A possible reason for this result was that the study stopped before the planned number of patients were recruited. Chen et al. [21] studied the pregnancy outcomes of single/double cleavage embryo transfers and single/double blastocyst transfers in patients with different delivery histories. They found that there were no differences in the clinical pregnancy or live birth rates between patients with previous CD or VD.

Additionally, Naji et al. [22] reported that the presence of a uterine scar affects the location of embryo implantation, with the mean distance between the embryo implantation site and the internal cervical os being 26.6 or 35.3 mm in women with previous CD or VD, respectively. As the implantation site approached the scar, the possibility of spontaneous abortion increased. Huang et al. [23] conducted a retrospective cohort study in women undergoing treatment using the freeze-all approach and also found that previous CD was associated with an increased risk of early miscarriage. However, in our study, the pregnancy loss rates of patients with different delivery histories after either SET or DET were similar, with previous CD not influencing the pregnancy loss rate.

Furthermore, our study suggested that CSD significantly reduced subsequent fertility in DET patients. After DET, the clinical pregnancy and live birth rates were significantly lower in patients with CSD than those without CSD. After SET, these rates also decreased, but the differences were not significant, except for CSD (compared to previous VD) significantly lowering the clinical pregnancy rate in the multivariate analysis. CSD may affect IVF-ET outcomes as follows: intrauterine fluid due to the CSD may impair embryo implantation, the CSD may alter the uterine immunobiology, uncoordinated/impaired uterine contractions may make embryo implantation difficult, the CSD may act as a physical obstacle against ET, and the CSD may affect the women's psychology and thus indirectly cause clinical symptoms [24]. Currently, there are no guidelines on the treatment of CSD. The main methods to treat CSD are medical treatments (oral contraceptives and intrauterine devices with levonorgestrel) and surgical treatments (hysteroscopic resection, laparoscopic repair, and vaginal repair) [15]. A study by Olivier et al. [25] showed

that laparoscopic repair for women who want to get pregnant can be considered as an appropriate method to reduce clinical symptoms and improve quality of life. Wang et al. [26] found that vaginal repair shortens the duration of menstruation. Vervoort et al. [27] treated CSD with hysteroscopic resection and found this method could reduce postmenstrual spotting and related symptoms. It has not been proved that one treatment method is superior to others. The selection should be made based on a comprehensive evaluation of the situation, including the wishes of the patient. Antila-Långsjö et al. [28] conducted a prospective cohort study and found that previous CD, a history of gestational diabetes, and high maternal BMI were independent risk factors for CSD development.

Our findings on neonatal birth weight may not have clinical significance due to the small sample size. Qin et al. [29] explored the relationship between previous CD and newborn birth weight in China. They found that the negative effects of previous CD on newborn birth weight were ameliorated by other factors such as the positive effects of the increased maternal body mass index, which occurred as the one-child policy was being brought to an end. Abenhaim et al. [30] reported that the newborns of women with previous CD were more likely to be born prematurely, develop respiratory distress syndrome, and require neonatal intensive care unit admission. Whether CD has specific effects on neonatal birth weight or other neonatal outcomes after FET needs further study.

The advantages of this study included the strict inclusion criteria, involving patients who had a history of only one parturition. Additionally, to accurately assess the effects of previous CD and CSD on pregnancy outcomes after IVF-FET, we excluded patients with various confounding factors that may affect pregnancy outcomes, such as patients with PCOS, adenomyosis, and other diseases. We used multivariate logistic regression to adjust for baseline characteristics that may differ among the three groups to reduce the influence of selection bias on the results.

The study also has certain limitations. First, it is only a single-center retrospective study. Although we reduced selection bias as much as possible, there are still known and unknown confounding factors that could not be adjusted for. For example, we did not collect information on the quality of transferred embryos, previous CD surgical methods, or the residual myometrial thickness. Moreover, TVS cannot identify all patients with CSD, so there will be missed cases, which may affect the results of the study.

In summary, among patients who received IVF-FET treatment, previous CD and the presence of a CSD reduced the success of clinical pregnancy and live birth, especially in DET patients. With the implementation of the universal two-child policy in China, the fertility rate of women with uterine scars will increase. Findings from this study add further evidence that the previous CD negatively affects pregnancy outcomes. It is recommended to avoid medically unnecessary primary CD. For infertile patients with a history of CD, if they desire to have a second child through IVF, it's important to get counseling before the cycle begins.

Conclusion

Our study's findings support that the previous CD negatively affects pregnancy outcomes. It is recommended to avoid medically unnecessary primary CD.

Abbreviations

CD: cesarean delivery; IVF: *in vitro* fertilization; FET: frozen-thawed embryo transfer; SET: single embryo transfer; CSD: Caesarean section defect; VD: Vaginal delivery; DET: double embryo transfer; TVS: transvaginal sonography; PCOS: polycystic ovary syndrome; BMI: body mass index; LH: luteinizing hormone; E2: estradiol; ORs: odds ratios; CIs: confidence intervals; FSH: Follicle-stimulating hormone

Declarations

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

Acknowledgements

The authors thank all the doctors, nurses, and embryologists in the Reproductive Medicine Center of Tianjin Central Hospital of Gynecology Obstetrics for their help in collecting data.

Authors' contributions

Yf Z contributed to the study design and wrote the manuscript. Dd Z contributed to study design and manuscript revision. XH and XT drafted the manuscript. YH contributed to revise the manuscript. JM collected the data. Ys Z contributed to editing the manuscript. HL critically revised the drafts of the manuscript. All authors reviewed the manuscript.

Funding

No funding was received.

Availability of data and materials

The data used or analyzed during the current study are included within the article. The datasets are not publicly available due to the hospital policy and personal privacy. However, the datasets are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Reproductive Center of Tianjin Central Hospital of Gynecology Obstetrics (No: ZY2021002) and performed in accordance with the Helsinki Declaration. All participating patients were informed that their clinical data may be used for academic research in the future before entering the IVF cycle and signed written informed consents.

Consent for publication

Not applicable.

Competing interests

No author has any potential confict of interest.

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Figures

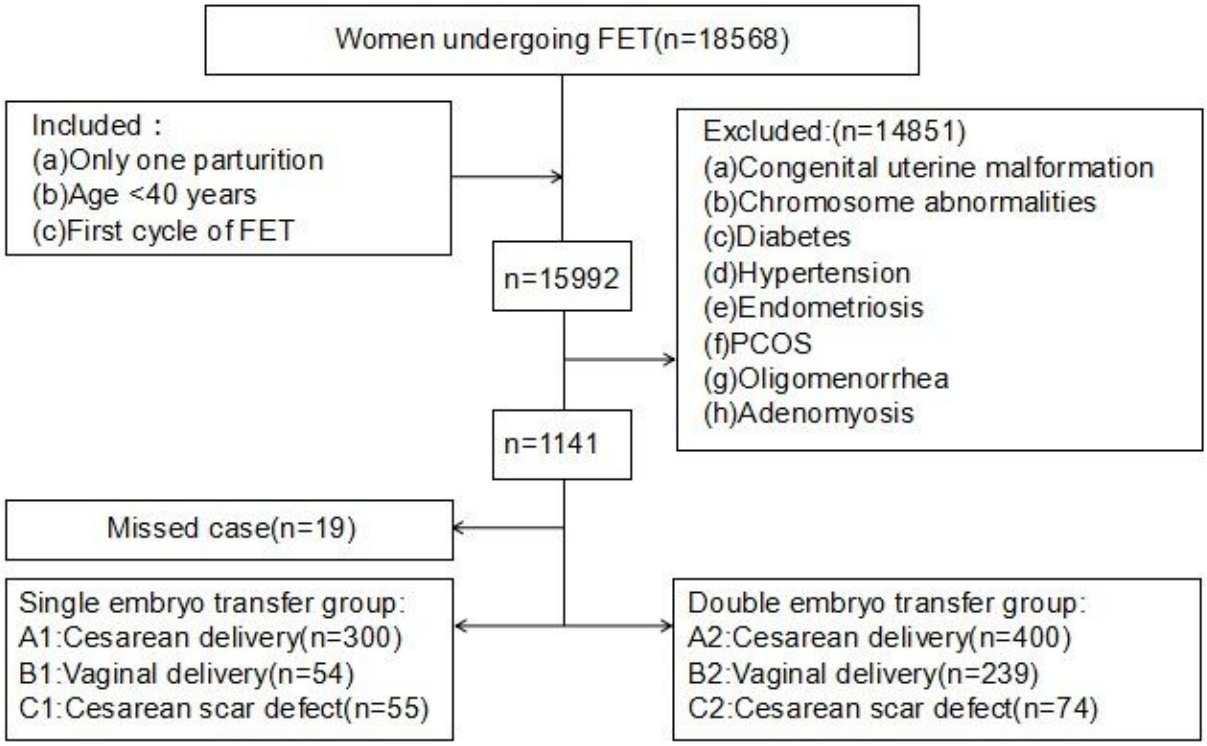

Figure 1

Flowchart of the study design.