IN FREEZE ALL EMBRYOS (FAE) CYCLES DUE TO ENDOMETRIAL FLUID (EF), LIVE BIRTH RATES IN SUBSEQUENT FROZEN EMBRYO TRANSFER (FET) ARE COMPARABLE TO THOSE OF CONTROLS, DESPITE HIGH RATES OF EF RECURRENCE AND CYCLE CANCELLATION

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INTRODUCTION

We aimed to compare the clinical outcomes of subsequent FETs between patients having had freeze-all embryos (FAE) for endometrial fluid (EF) and controls having had a FAE for other indications, including the recurrence rate of EF and live birth rates (LBR) during subsequent frozen cycles.

DESIGN

A retrospective cohort study including all patients with freeze-all cycles for endometrial fluid at a university-affiliated private IVF center between 2010 and 2016.

METHODS

Controls were randomly generated from freeze-all cycles for other indications during the same period. Gestational carriers, patients undergoing PGS/PGD cycles, or egg donation cycles, patients having no embryo to transfer or hydrosalpinx were excluded.

The primary outcome was cumulative LBR (CLBR) per started FET cycle and per patient.

Secondary outcomes included EF recurrence rate, cycle cancellation rate, pregnancy rate (PR) and pregnancy loss rate.

Between-group differences were ascertained with Chi-Square or Student's t-test, as appropriate.

RESULTS

Table 1. Population characteristics, first FET cycle (n=302)

	Patients with FAE for EF (n=83)	Controls (n=219)	*p* value
Age	34.7	34.4	0.64
Day 3 AFC	20.5	23.7	0.06
Day 3 AMH (ng/ml)	3.90	4.44	0.39
Cause of FAE, n(%)			
- Endometrial fluid	83 (100)	0 (0)	
- OHSS	0 (0)	101 (46.1)	
- Elevated PG	0 (0)	82 (37.4)	-
- Uterine cause	0 (0)	20 (9.1)	
- Others	0 (0)	16 (7.3)	
Number of frozen embryo	3.95	3.88	0.84
- Day 3 embryos	2.7	2.05	0.07
- Blastocysts	1.14	1.48	0.25
Number of remaining embryos	1.11	0.85	0.31
≥ 1 Blastocyst, n(%)	28 (33.7)	87 (39.7)	0.36

AFC: antral follicle count at Day 3; AMH: anti Müllerian hormone; PG, progesterone

A total of 83 patients with FAE cycles for EF and 219 controls were included. Population characteristics were comparable between the two groups. In controls, the indications for FAE included OHSS (46%), elevated progesterone (37%), uterine causes (9.1%) and other (7.3%).

The EF rate in 3 subsequent FET cycles was significantly higher in the study group compared to the control group: 15.7% vs. 0.5% (p<0.001); 22.9% vs. 0% (p<0.001); 17.3% vs. 1.8% (p=0.02).

Cancellation rates in subsequent FET cycles were significantly higher in the study group compared to the control group: 18.1% vs. 4.1% (p<0.001), 22.9% vs. 8.5% (p=0.02).

Table 2. Freeze-all cycle cumulative outcomes (n=302)

	Cases of EF (n=83)	Controls (n=219)	*p* value
Mean number of FET cycles	2.16 ±1.5	2.01 ± 1.3	0.40
Mean total number of embryo transferred per patient	2.49 ± 1.8	2.43 ± 1.5	0.79
Recurrence of endometrial fluid per FET cycle, n(%)	33/177 (18.6)	5/441 (1.1)	< 0.001
Cancellation %			
- per FET	35/177 (19.8)	36/441 (8.2)	< 0.001
- per patient	35/83 (42.2)	36/219 (16.4)	< 0.001
Biochemical pregnancy, n(%)			
- per FET	61/177 (34.5)	149/441 (33.8)	0.87
- per patient	61/83 (73.5)	149/219 (68)	0.36
Clinical pregnancy per FET cycle, n(%)	49/177 (27.7)	127/441 (28.8)	0.78
Live birth, n(%)			
- per FET cycle	33/177 (18.6)	103/441 (23.4)	0.20
- per patient	33/83 (39.8)	103/219 (47)	0.26
Number of necessary FET to have a LB	5.4	4.3	0.20

The PR, pregnancy loss rate and LBR were comparable between the two groups. However, in patients with FAE for EF presenting with at least one EF recurrence during subsequent FETs, cumulative PR per FET cycle was 16.4% and CLBR per FET cycle was 5.4%.

CONCLUSIONS

Despite higher rates of EF recurrence and cycle cancellation, patients with FAE for EF ultimately have comparable pregnancy and LBR to those having had a FAE for other indications. Nonetheless, patients presenting with at least one EF recurrence during subsequent FETs seem to have lower PR and LBR.