TWO FOR THE PRICE OF ONE: TWINS AND MULTIPLE BIRTHS FOLLOWING A NATURAL VS PROGRAMMED SINGLE FROZEN BLASTOCYST TRANSFER CYCLE

Alison J. Meyers[1,2]; Virginia Mensah[2] ; Brittany Morse[1]; Denny Sakkas[1]; Denis Vaughan[1,3,4]

[1]Boston IVF - IVIRMA Global Research Alliance, Waltham, Massachusetts
[2]The Warren Alpert Medical School of Brown University, Providence, Rhode Island
[3]Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, Massachusetts
[4]Department of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School, Boston, Massachusetts

BACKGROUND AND OBJECTIVE

The use of single Frozen Embryo Transfers (sFETs) has led to a virtual elimination of multiple pregnancies. In some cases, however, transferring a frozen embryo in a natural cycle can lead to twins from the frozen embryo transfer and a natural ovulation.

THE OBJECTIVE OF THIS STUDY IS TO COMPARE THE INCIDENCE AND ZYGOSITY OF TWINS AND HIGHER ORDER MULTIPLES IN MODIFIED NATURAL COMPARED TO PROGRAMMED sFETS, SO AS TO FACILITATE APPROPRIATE COUNSELING OF PATIENTS REGARDING THE IMPORTANCE OF ABSTINENCE DURING NATURAL AND SEMI-NATURAL sFET CYCLES TO REDUCE THIS MULTIPLES RISK.

METHODS

- Retrospective cohort study of sFET twin and higher-order multiples pregnancies from U.S.-based Boston IVF clinics
- Deidentified data extracted from a single electronic medical record database (eIVF). Medical records from August 2013 to April 2024 were reviewed. Patients of maternal age 18-43 who underwent an autologous sFET cycle and had a confirmed twin or higher-order multiple pregnancy were included in final analysis
- Comparisons made using the chi-square test for categorical variables and parametric OR non-parametric tests for continuous variables based on data distribution
- GEE model clustered by patient was used (to account for the correlation of patients that had more than 1 transfer cycle) to predict the outcomes
- All tests were two sided and a P value <0.05 was required to confer significance

RESULTS

- 283 patients were included (Figure 1)
- There is a significant difference in the likelihood of pregnancies leading to two or more fetuses in the natural cycle group vs. programmed (p = 0.045, chi-squared = 4.01)
- Using OR analyses, the odds of achieving twins or higher-order multiples are lower for programmed compared to natural cycles (OR=0.59, CI 95% (0.36-0.96))
- These findings remain consistent when adjusting for age at transfer and number of fetal sacs
- Further research is needed to confirm that the higher rate of twins/multiples in the natural cycle group is due to concurrent natural conception

FIGURES & TABLES

Figure 1: Flowchart of sFET outcomes during study period resulting in singleton and multiple pregnancies

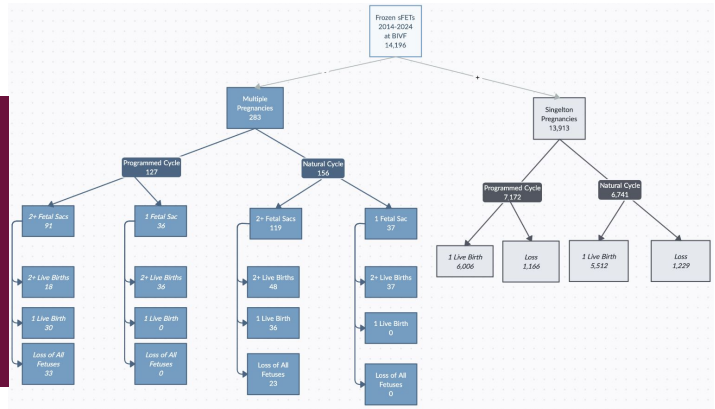

Table 1: Comparison of programmed cycle vs. natural cycle sFETs. Bolded values represent statistically significant findings

Variable	P value	Unadjusted OR for Natural Cycle Twin Pregnancies vs. Programmed Cycle Twins	95% CI	Chi Squared	Adjusted OR for Age at Retrieval (95% CI)
All Twin Pregnancies	**0.045**	**0.59**	**0.36-0.96**	**4.01**	**0.57 (0.34-0.95)**
Live Births Only	0.48	0.77	0.43-1.39	**9.89**	0.73 (0.39-1.36)
All Pregnancies from 2+ Fetal Sacs	**0.002**	**0.34**	**0.18-0.66**	0.49	**0.36 (0.18-0.71)**
Live Births Only from 2+ Fetal Sacs	**0.047**	**0.45**	**0.22-0.93**	**3.93**	**0.45 (0.21-0.98)**

CONCLUSIONS

- sFETs have the goal of a singleton pregnancy for patients undergoing ART treatments for infertility
- There is an unavoidable risk of monozygotic twinning, occurring at frequency of about 2%[1]
- Patients who have intercourse during their natural sFET cycle may inadvertently increase their risk of fraternal twin (or multiples) conception[1,2]

IMPACT STATEMENT

The data show that the incidence of twins and higher-order multiples is significantly higher in natural cycle compared to programmed cycle sFETs. With this data, providers can facilitate appropriate counseling of patients regarding the importance of abstinence during natural and semi-natural sFET cycles to mitigate the risks that come with multiple gestations.

NEXT STEPS

Survey patients who underwent natural cycle sFETs and had twins/multiples to confirm zygosity and inquire about possible concurrent natural conception during sFET cycle. A subset of programmed cycle sFETs with twin/multiples outcomes will be contacted as controls.

REFERENCES

1. Mateizel I, Santos-Ribeiro S, Done E, et al. Do ARTs affect the incidence of monozygotic twinning? Hum Reprod. 2016;31(11):2435-2441. doi:10.1093/humrep/dew216
2. Vaughan DA, Seidler EA, Murphy LA, et al. Double trouble? Clinic-specific risk factors for monozygotic twinning. Fertil Steril. 2020;114(3):587-594. doi:10.1016/j.fertnstert.2020.04.010

BOSTON IVF · IVIRMA Global · HARVARD MEDICAL SCHOOL · BROWN Alpert Medical School