# TUBAL EVALUATION IN THE DIAGNOSTIC EVALUATION OF PATIENTS WITH UNEXPLAINED RECURRENT PREGNANCY LOSS (RPL) UNDERGOING SINGLE, EUPLOID FROZEN EMBRYO TRANSFER (FET): A RETROSPECTIVE COHORT STUDY

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## INTRODUCTION

Recurrent pregnancy loss (RPL) is defined as two or more pregnancy losses, excluding molar or ectopic pregnancies. Beyond diagnosis, it can often be challenging to identify a cause.

- Assessment of couples with RPL focuses on screening for genetic factors, antiphospholipid syndrome, abnormal uterine anatomy, hormonal and metabolic factors, and lifestyle variables.

Uterine anatomy assessment is widely recommended even though the role of abnormalities in RPL is questionable.

- Workup can start with a hysterosalpingogram (HSG) or saline sonogram (SIS) and then can be further characterized by MRI or 3D ultrasound, if indicated.
- There is no definitive recommendation of HSG or SIS as first-line for this evaluation.

Interestingly, even though tubal factor is not a part of the typical workup of RPL, an HSG can identify tubal pathology and clarify diagnoses. It is unclear what the incidence of tubal pathology is in this population, if this impacts outcomes for those undergoing an embryo transfer, and therefore whether this additional evaluation adds value to the workup of RPL.

## OBJECTIVE

In the work up of RPL, an HSG or SIS can be performed for uterine cavity evaluation. There is no indication for identifying tubal pathology and it is unclear whether tubal pathology adds to the RPL evaluation. This study aimed to compare FET outcomes in those with unexplained RPL based on presence of HSG findings.

## METHODS

First single, euploid FET in 02/2017 - 06/2024 of patients with unexplained RPL at an academic-affiliated center were included.

Cycles were categorized by cavity method evaluation:

1. SIS only
2. SIS and HSG, stratified by tubal results (normal and abnormal)

Primary outcome:

- Sustained implantation rate (SIR, presence of fetal cardiac activity at 8-9 weeks)

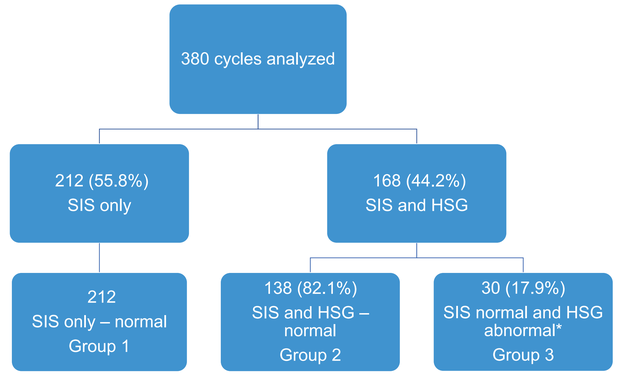
Secondary outcomes:

- Biochemical pregnancy rate (bHCG >3 mIU/ml)
- Clinical pregnancy rate (CPR, presence of gestational sac)
- Live birth rate (LBR)
- Pregnancy loss rate

Comparisons between groups were performed using ANOVA for continuous variables and Fischer's exact and Chi-square tests for categorical variables. Logistic regression models adjusted for oocyte age, body mass index, and day of blastulation.

## RESULTS

**FIGURE 1. Patient inclusion flow diagram.**



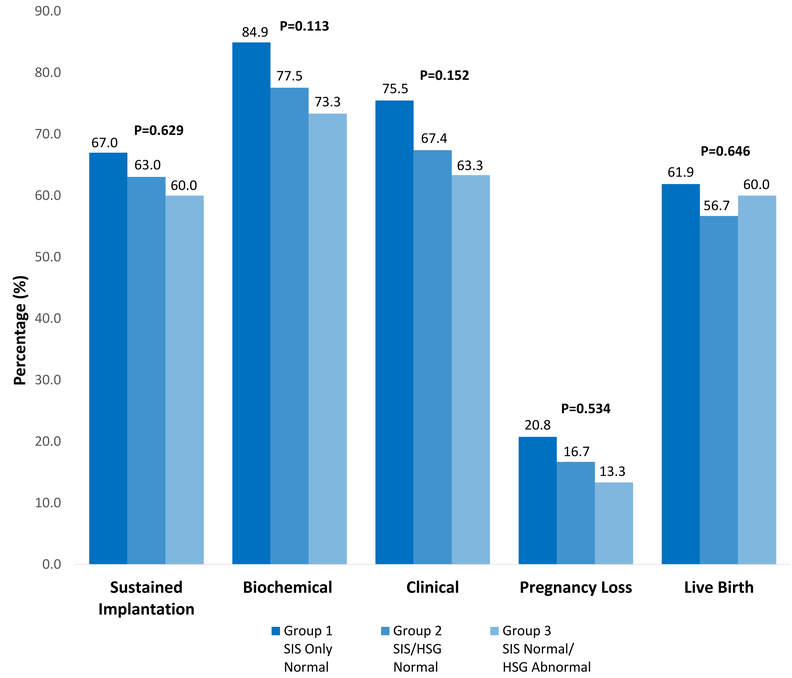

*Abnormal tubal findings included cases with unilateral/bilateral proximal tubal obstruction, patent tube with distal dilation, patent tube with loculated spill. One case had a non-patent tube with distal dilation.

**TABLE 1. Baseline Characteristics of FET Cycles.**

| Variables | Group 1 SIS Only Normal (n=212) | Group 2 SIS/HSG Normal (n=138) | Group 3 SIS Normal/ HSG Abnormal (n=30) | P-value |
|---|---|---|---|---|
| **Age at Transfer (years)** | 36.3 ± 3.9 | 35.2 ± 3.7 | 35.0 ± 4.5 | 0.014 |
| **Oocyte Age (years)** | 36.1 ± 3.9 | 34.9 ± 3.7 | 34.8 ± 4.5 | 0.013 |
| **BMI (kg/m²)** | 26.0 ± 5.1 | 26.2 ± 5.3 | 27.4 ± 5.4 | 0.366 |
| **Transfer Protocol** | | | | 0.884 |
| Modified Natural | 35 (16.5) | 23 (16.7) | 3 (10) | |
| Stimulated | 6 (2.8) | 4 (2.9) | 0 (0) | |
| Programmed | 171 (80.7) | 111 (80.4) | 27 (90) | |
| **Serum Estradiol Level Prior to Progesterone Exposure (pg/mL)** | 439.9 ± 585.4 | 325.8 ± 350.2 | 406.0 ± 276.1 | 0.107 |
| **Endometrial Thickness Prior to Progesterone Exposure (mm)** | 9.1 ± 1.8 | 9.1 ± 1.8 | 9.2 ± 1.9 | 0.944 |
| **Serum Progesterone Level Prior to Transfer (ng/mL)** | 23.6 ± 9.4 | 23.1 ± 10.2 | 23.7 ± 11.9 | 0.892 |
| **Day of Blastulation** | | | | 0.120 |
| 5 | 100 (47.2) | 54 (39.1) | 10 (33.3) | |
| 6 | 109 (51.4) | 77 (55.8) | 19 (63.3) | |
| 7 | 3 (1.4) | 7 (5.1) | 1 (3.3) | |
| **SART Grade** | | | | 0.670 |
| Good | 91 (42.9) | 61 (44.2) | 11 (36.7) | |
| Fair | 109 (51.4) | 71 (51.4) | 19 (63.3) | |
| Poor | 12 (5.7) | 6 (4.3) | 0 (0) | |

Data are presented as mean (SD) for all continuous variables and number (%) for categorical variables.

**Figure 2. Pregnancy outcomes by method of RPL cavity evaluation.**




Post-hoc analysis revealed significant differences in patient age at time of transfer and oocyte age between the SIS only-normal group and the HSG/SIS-normal group (p = 0.022 and p = 0.021, respectively).

No cycles had an exploratory laparoscopy prior to their first FET.

The overall SIR was 65%.

After adjustment for oocyte age, BMI, and day of blastulation, there was no association between uterine cavity classification and pregnancy or live birth outcomes.

## CONCLUSION

**In patients with unexplained RPL who underwent an HSG prior to a FET and had tubal pathology present compared to those with normal HSG findings and to those with only an SIS, there was no difference in the first single euploid FET outcomes.**

**Even though there is no definitive recommendation on the method of uterine cavity evaluation in RPL, HSGs do not appear to provide additional benefit compared to the more tolerated SIS, which has better sensitivity and specificity for uterine pathology.**