

HOW SOON IS TOO SOON: ANALYZING THE IMPACT OF INTERPREGNANCY INTERVAL (IPI) ON SINGLE EUPLOID FROZEN EMBRYO TRANSFER CYCLE (SEFET) OUTCOMES

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Background: A short interpregnancy interval, defined as duration of time (in months) between delivery of one pregnancy and conception of a subsequent pregnancy, is known to be associated with poor perinatal outcomes including preterm delivery, low birth weight, and small for gestational age [1]. Some studies have examined pregnancy outcomes of single FET cycles occurring at varying interpregnancy intervals, and have found that although there may be no difference in live birth rate (LBR) in shorter (< 12 months) interpregnancy intervals, there may be higher preterm birth rates [2,3]. However, a different study looked at outcomes from single FET specifically after cesarean delivery, and found no significant differences in the proportion of live births or mean gestational age at time of delivery across different interpregnancy intervals [4]. Furthermore, while it is widely accepted that shorter interpregnancy intervals are associated with increased maternal morbidity including gestational diabetes, precipitous labor, and placental abruption, it remains unclear if this is true for single FET IVF pregnancies [5].

Objective: The purpose of this study was to assess IPI's impact on live birth rate (LBR) and perinatal outcomes in SEFET.

Materials and Methods: This retrospective cohort study at an academic-affiliated in vitro fertilization (IVF) center analyzed all SEFETs (2017-2023) in patients with a prior full-term live birth resulting from an FET. Patients were grouped by IPI, the time from delivery of the first pregnancy to the subsequent FET in months (< 12, 12-18, 18-24, > 24) with a subgroup analysis for IPIs <12 months (<9, 9-12). The primary outcome was LBR; secondary outcomes included clinical pregnancy rate (CPR), ectopic pregnancy, pregnancy loss, cesarean delivery, preterm delivery, and other complications including placental abruption, placenta previa, gestational diabetes, and pregnancy-induced hypertension. Categorical variables were analyzed using Chi-Square and Fisher Exact tests, and continuous variables with ANOVA and proportion tests. Rates were reported as percent [95% CI].

Results: A total of 2,167 patients were included. Apart from older age in longer IPI groups, there were no demographic differences. After controlling for baseline cycle characteristics, we found no difference in LBR between IPI groups (<12 months: 68.4% [62.6, 73.6]; 12-18 months: 68.1% [64.8, 71.3]; 18-24 months: 67.4% [63.3, 71.2]; >24 months: 65.0% [61.0, 68.7]; $p = 0.62$). None of the secondary outcomes, including CPR, ectopic pregnancy and pregnancy loss rates, cesarean delivery rates, preterm delivery rates, nor pregnancy complications differed between IPI groups.

In the <12 month subgroup analysis, LBR was significantly higher in the 9-12 month group compared to the < 9 month group ($p = 0.04$) (Table 1). This finding may be influenced by the significantly higher trophoctoderm grades in the 9-12 month group ($p = 0.01$). No other significant differences were seen in baseline characteristics or pregnancy outcomes (Table 1).

Conclusions: Pregnancy outcomes may be comparable after consecutive SEFETs with IPIs of ≥ 9 months, though LBR may decrease with IPI < 9 months. In an infertility population that is often anxious to proceed with treatment, this data is reassuring that an IPI of at least 9 months is protective of obstetrical outcomes.

Support: None

References:

1. Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. *Birth spacing and risk of adverse perinatal outcomes: a meta-analysis*. JAMA. 2006;**295**(15):1809-1823.
2. Palmor M, Eliner Y, Shah JS, et al. *Short interpregnancy interval (IPI) does not decrease live birth rates among patients undergoing subsequent frozen embryo transfer (FET)*. Fertil Steril. 2021;**116**(3 Suppl).
3. Quinn MM, Rosen MP, Allen IE, Huddleston HG, Cedars MI, Fujimoto VY. *Interpregnancy interval and singleton pregnancy outcomes after frozen embryo transfer*. Fertil Steril. 2019;**111**(6):1145-1150.
4. Zalles LX, Le K, Jahandideh S, et al. *Impact of time interval from cesarean delivery to frozen embryo transfer on reproductive and neonatal outcomes*. Fertil Steril. 2024;**122**(3):455-464.
5. Hutcheon JA, Nelson HD, Stidd R, Moskosky S, Ahrens KA. *Short interpregnancy intervals and adverse maternal outcomes in high-resource settings: An updated systematic review*. Paediatr Perinat Epidemiol. 2019;**33**(1):O48-O59.

Table 1. Pregnancy outcomes in IPI < 12 months

Outcome	< 9 months (n=71) % [95% CI]	9-12 months (n=201) % [95% CI]	P-value
Clinical pregnancy	79.0 [66.7, 87.5]	85.7 [79.8, 90.1]	0.32
Pregnancy loss	21.4 [13.4, 32.4]	14.5 [10.3, 20.1]	0.24
Live birth	57.8 [46.2, 68.6]	72.1 [65.6, 77.9]	0.04*
Full term delivery	90.2 [77.5, 96.1]	97.2 [93.1, 98.9]	0.07
Cesarean delivery	39.0 [25.7, 54.3]	43.8 [35.9, 51.9]	0.72
Gestational diabetes	7.0 [2.8, 16.7]	6.3 [3.6, 10.9]	0.77

* statistical significance (p < 0.05)