

**Title:** Does Interval Between Breastfeeding Cessation and Frozen Embryo Transfer (FET) Cycle Affect Outcomes?

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**Background:** The rise in prolactin (PRL) secretion while breastfeeding interferes with the hypothalamic-pituitary-ovarian (HPO) axis. While there appears to be PRL receptors in the endometrium, the impact of rising PRL during breastfeeding on endometrial receptivity remains unknown.

**Objective:** The purpose of this study was to assess whether the time interval from cessation of breastfeeding to initiation of a frozen embryo transfer (FET) cycle correlates with pregnancy outcome.

**Materials & Methods:** This study included patients from January 2012 to December 2022 who stopped breastfeeding within 12 months of an FET cycle. Patients were grouped by time interval: Group 1: patients who stopped breastfeeding  $\leq$  1 month; Group 2: 1-3 months; Group 3: 3-7 months; Group 4: 7-12 months prior to start of an FET cycle. Age, anti-mullerian hormone (AMH), body mass index (BMI), endometrial thickness, PRL level prior to FET cycle initiation, use of pre-implantation genetic testing for aneuploidy (PGT-A) and embryo quality were compared between groups. Comparative statistics were performed using Kruskal-Wallis and chi-square. Multivariate logistic regression was performed to compare the odds of pregnancy, clinical pregnancy, loss, and live birth between groups.

**Results:** A total of 197 patients met inclusion criteria: Group 1: 54, Group 2: 58, Group 3: 46, Group 4: 39. There was no significant difference in characteristics between the groups for any variables. On univariate analysis, there was no statistically significant difference in pregnancy rate between groups 1, 2, 3, and 4 (79.6% vs 72.4% vs 78.2% vs 87.1%,  $p = 0.38$ ). When adjusted for variables, with Group 4 as reference, there was no difference in odds of pregnancy based on timing from cessation of breastfeeding to initiation of FET (1 vs 4: OR 0.41, CI 0.11-1.56,  $p=0.19$ , 2 vs 4: OR 0.92, CI 0.33-2.55,  $p= 0.87$ , 3 vs 4: OR 0.417, CI 0.11-1.56,  $p=0.19$ ). Similarly, there was no statistically significant difference in odds of clinical pregnancy, pregnancy loss, or ongoing clinical pregnancy.

**Conclusions:** Patients who stopped breastfeeding within 12 months of initiating an FET cycle had no difference in clinical pregnancy rates. Patients and providers can be reassured that outcomes of FET cycles are similar regardless of interval from breastfeeding cessation, suggesting there is no negative effect on embryo implantation. Overall, breastfeeding cessation within 12 months of frozen embryo transfer cycle initiation does not seem to be associated with adverse pregnancy outcomes.

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	<b>Group 1 (n= 54)</b>	<b>Group 2 (n=58)</b>	<b>Group 3 (n=46)</b>	<b>Group 4 (n=39)</b>	<b>p value</b>
<b>Pregnancy Rate (%)</b>	79.6	72.4	78.2	87.1	0.38
<b>Biochemical Loss Rate (%)</b>	20.9	21.4	13.8	29.4	0.47
<b>Clinical Pregnancy Rate (%)</b>	62.9	56.9	67.3	61.5	0.75
<b>Clinical Pregnancy Loss Rate (%)</b>	20.5	12.1	16.1	12.5	0.77
<b>Live Birth Rate (%)</b>	51.8	50	56.5	56.4	0.88