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**SINGLE EUPLOID EMBRYO TRANSFER OUTCOMES IN PATIENTS WITH A HISTORY OF CANCER TREATMENT: IS THERE A LONG-TERM EFFECT OF CHEMOTHERAPY BEYOND GONADOTOXICITY?**

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**OBJECTIVE:**

Systemic chemotherapy may impair future reproductive potential due to the long-term gonadotoxic effects on ovarian function. To proactively manage this risk, patients have the option to delay family building by cryopreserving oocytes and/or embryos for future use in frozen-thawed transfer cycles. However, there is limited data on whether chemotherapy affects other aspects of reproduction, particularly uterine receptivity. This study aims to evaluate pregnancy outcomes in patients with a history of chemotherapy who undergo single euploid embryo transfer (SEET).

**MATERIALS AND METHODS:**

This retrospective cohort study was conducted at a single, academic affiliated fertility center, and included all patients with a history of chemotherapy who subsequently underwent a SEET from 2011 to 2023. Patient cycles with a history of chemotherapy were matched with controls by oocyte age, patient age at SEET, BMI, year of SEET, and oocyte source (autologous versus donor). Descriptive statistics and univariate analyses were performed using Wilcoxon-Rank and chi-square. Logistic regression fitted with GEE controlling for confounders was performed to determine the association between a history of chemotherapy and pregnancy, clinical pregnancy, clinical pregnancy loss (CPL), and ongoing pregnancy/live birth (OP/LB).

**RESULTS:**

A total of 64 cycles from 33 patients with a history of chemotherapy were included and matched 1:3 to 192 control cycles. In the post chemotherapy group, 25.0% (n=16) used autologous oocytes/embryos frozen prior to chemotherapy, 26.6% (n=17) used donor oocytes and 48.4% (n=31) used autologous oocytes after chemotherapy. Oocyte age in this group was  $33.0 \pm 5.5$  and age at SEET was  $38.2 \pm 5.7$ . The difference in endometrial thickness was



statistically significant, with inner lining in patients who underwent chemotherapy than in controls (median: 8mm vs 9mm, respectively;  $p=0.02$ ). OP/LB rate was 43.8% with a history of chemotherapy and 52.1% in controls. CPL was 25.0% with prior chemotherapy versus 12.9% in controls. Logistic regression model showed the odds of pregnancy (OR 0.46 CI 0.29-0.71  $p<.001$ ) and OP/LB (OR 0.40, CI 0.24-0.38 $p<0.001$ ) were significantly lower in patients with a history of chemotherapy, while odds of CPL (OR2.45, CI 1.14 – 5.24) was higher compared to controls ( $p=0.02$ ).

#### **CONCLUSIONS:**

Patients who previously underwent chemotherapy have significantly lower odds of pregnancy and OP/LB and higher odds of CPL after SEET compared to patients without a history of chemotherapy. Suboptimal pregnancy outcomes may be explained by the effect of chemotherapy on the endometrium, perhaps related to deleterious effects on progenitor stem cells in the stratum basalis, myometrium, uterine vasculature, or gene expression (1). Understanding these mechanisms may facilitate more targeted treatment with a precision medicine-based approach.

#### **IMPACT STATEMENT:**

While fertility preservation and future reproductive options exist for patients faced with the need for chemotherapy, more data is needed to explore the potential effect of chemotherapy beyond gonadotoxicity.

#### **REFERENCES:**

1. Griffiths, M. Winship, A. Hutt, K. Do cancer therapies damage the uterus and compromise fertility? Human Reproduction Update, Vol.26, No.2, pp. 161–173, 2020