TITLE: MATERNAL OUTCOMES OF FIRST PREGNANCY AFTER CHEMOTHERAPY FOR GESTATIONAL TROPHOBLASTIC NEOPLASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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INTRODUCTION: Patients who have completed chemotherapy for gestational trophoblastic neoplasia (GTN) often express concerns about future pregnancies. While cytotoxic drugs are potentially mutagenic and teratogenic, previous research has suggested that GTN patients can expect normal reproductive outcomes. However, there is limited data specifically focusing on the first pregnancies following chemotherapy, which may carry unique risks for maternal morbidity.

OBJECTIVE: To determine the prevalence of maternal outcomes in the first pregnancy following chemotherapy for gestational trophoblastic neoplasia.

METHODS: A search was conducted using Subject Headings related to maternal outcomes, chemotherapy, and GTN included references up to 31/10/25 in Embase, LILACS, MEDLINE, CENTRAL and Web of Science. Inclusion criteria were observational cohort studies evaluating maternal outcomes of first pregnancies after chemotherapy for GTN. Specific outcomes included ectopic pregnancy, hypertension, diabetes, placenta accreta, placenta previa, recurrent molar pregnancy, post-gestational choriocarcinoma, and spontaneous abortions. Exclusion criteria were animal studies, interventional studies, narrative reviews, expert opinions and studies with previous treatments introducing confounding bias. Two independent reviewers screened references and extracted data. Meta-analysis was performed using bivariate random-effects models. Publication bias was assessed via funnel plots or Egger's test. Statistical significance was set at $P<.05$. PROSPERO/ CRD42022350964/2018.

RESULTS: Literature search identified 4238 studies, of which 77 underwent full-text eligibility assessment, 7 observational cohort studies met the inclusion criteria and were included in the systematic review and meta-analysis. These studies encompassed data from 7726 participants, reporting 1627 first pregnancies after chemotherapy for GTN. Miscarriage was the most frequently reported maternal outcome. Meta-analysis revealed a pooled prevalence of any maternal outcome of 16% (95% CI: 10% to 26%) using random effects model. Significant heterogeneity was observed among the studies (I^2=80%, $p<0.01$). Individual study prevalences ranged from 3% to 43%. Egger's test ($p = 0.63$) did not suggest funnel plot asymmetry, indicating no evidence of publication bias.

CONCLUSION: The prevalence of maternal outcomes in the first pregnancy after chemotherapy for GTN appears comparable to general population. However, this conclusion is tempered by significant limitations, particularly the lack of comprehensive reporting of maternal outcomes across studies. We strongly advocate for improved reporting practices in future research. To address the limitations identified in this analysis, further studies are needed.