

Assisted Reproductive Technology Outcomes in Childhood Cancer Survivors: A Report from the Childhood Cancer Survivor Study

Background Some treatment exposures for childhood cancer reduce ovarian reserve. Registry-based evaluation has not been conducted for assisted reproductive technology (ART) outcomes of female survivors.

Methods The Childhood Cancer Survivor Study, a retrospective cohort of five-year survivors and siblings, was linked to the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), which captures nationwide, CDC-required reporting of ART outcomes. We assessed live birth rate and relative risk (RR, 95% CI) as a function of treatment exposure, using generalized estimating equation to account for multiple ovarian stimulations per subject.

Results Among 9885 female survivors, 137 (1.4%; median age at diagnosis 10 years, range 0-20; 11 years of follow-up, 2-11) underwent 243 ART cycles (mean 1.8 cycles) and among 2419 siblings, 33 (1.4%) underwent 60 ART cycles (mean 1.8). Median age at autologous egg retrieval was 30 years (19-44) for survivors and 34 (24-43) for siblings. In the subset using autologous eggs (Table), 99 survivors underwent 155 ovarian stimulation cycles that resulted in 113 embryo transfers and 49 live births for a live birth rate of 32% per ovarian stimulation and 43% per transfer. Sibling live birth rate was 38% ($p=0.39$ compared to survivors) per autologous ovarian stimulation and 53% ($p=0.33$) per transfer. 38 survivors and 1 sibling underwent egg donor ovarian stimulation cycles. Two survivors used autologous eggs with gestational carriers and one cycle resulted in live birth. Cranial radiation therapy (RT) [RR 0.48 (0.27-0.87) $p=0.02$] and pelvic RT [0.30 (0.14-0.66) $p=0.002$], compared with no RT, resulted in lower RR of live birth in survivors. The likelihood of live birth after ART in survivors was not impacted by alkylator exposure [CED<8000 mg/m² vs. none: 1.14 (0.65-2.02); CED \geq 8000 mg/m² vs none: 1.07 (0.06-1.91)].

Conclusion While live birth rates among survivors were lower compared with siblings, differences were not statistically significant. Pelvic and cranial RT were associated with a decreased likelihood of live birth, with no association with alkylator exposure identified.

Diagnosis	Ovarian stimulations (N=155)	Embryo transfer (N=113)	Live birth per ovarian stimulation (N=49)
Neuroblastoma	14	14	9(64%)
Bone cancer	15	10	7(47%)
Soft tissue sarcoma	9	5	4(44%)
CNS	12	8	5(42%)
Kidney (Wilms)	16	10	5(31%)
NHL	10	6	3(30%)
Leukemia	40	29	9(23%)
HD	39	31	7(18%)