

Effect of hypothalamic/pituitary radiation exposure in low doses on fertility in female childhood cancer survivor study (CCSS) participants.

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Abstract:

Background: Female childhood cancer survivors (CCS) are less likely to report having been pregnant when compared with females within the CCSS sibling cohort (Sibs) as the result of direct damage to the ovaries produced by radiation therapy (XRT) and/or chemotherapy. High-dose hypothalamic/pituitary (HPT) XRT, which causes central or secondary hypogonadism, may result in infertility due to failure to stimulate ovulation. Recently, another possible central mechanism has been postulated, luteal phase deficiency, resulting from low-dose HPT XRT.

Methods: We evaluated the occurrence of pregnancy in 3,666 female CCS who participated in the CCSS and 2,082 Sibs. The association between low- dose HPT XRT and fertility was studied by restricting analyses to those female CCS who received no/scatter (≤ 10 cGy) radiation to the ovaries and comparing their fertility rates with those of Sibs using Cox-proportional hazards models. Specific treatment effects were studied by further limiting analyses to only CCS. **Results:** These CCS who received no/scatter (≤ 10 cGy) ovarian radiation were more likely to report being pregnant (hazard ratio [HR]:1.5, 95% confidence interval [95%CI]: 1.3, 1.7) when adjusted for race/ethnicity, smoking, marital status, and education than Sibs. Multivariable models showed a significant decrease in the risk of reporting pregnancy with HPT XRT doses of $\geq 2,200$ cGy when compared with those CCS receiving no HPT XRT when adjusted for race/ethnicity, smoking, marital status, education, age at diagnosis, and treatment with VP16 (Table) (137 had missing HPT radiation doses). **Conclusions:** The results of this study support the hypothesis that low-dose HPT XRT may be a contributing factor to infertility among female CCS.

HPT radiation dose (cGy)	Number of CCSS participants	HR ever pregnant	95% CI ever pregnant
0	1,996	1.0	
> 0 to < 1500	371	0.8	0.7-1.1
≥ 1500 to < 2200	599	0.9	0.7-1.1
≥ 2200 to < 2700	316	0.6	0.5-0.8
≥ 2700	247	0.7	0.5-0.9