

# Z-SCORES FOR COMPARATIVE ANALYSES OF FOLLICULAR DENSITY IN OVARIAN CORTEX AMONG CHILDREN AND YOUNG ADULTS

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## **Abstract Body**

Female fertility is dependent on the number of primordial follicles in the ovary, i.e., the ovarian reserve. Menopause starts when the reserve is depleted to the point it cannot sustain hormone secretion required for normal ovarian function. The size of the reserve depends on several factors, including age, genetic conditions, and chemical exposures. Fertility preservation is an important service for women receiving gonadotoxic treatments. For pre-pubertal patients, ovarian tissue cryopreservation (OTC) is the only option to preserve fertility. The success of OTC depends on the number of follicles present in the ovarian cortical tissue. Therefore, having reference data for normal follicular densities (FDs) in an age-dependent manner would be of great value when quality of cryopreserved ovarian tissue is evaluated.

Here, we conducted a review of published quantitative histological data of follicle numbers in the cortex (1mm from surface epithelium) in girls and women with no known ovarian pathologies, aged 0-24 years old, to create normal ovarian reference model. Furthermore, we collected histological data of ovarian tissue from 153 girls representing various pathologies to test the Z-score model. This data includes FDs of biobank (non-cancer patients), archived (cancer patients) and published materials (cancer, hematological disease and Turner's syndrome patients). The treated cancer patients were further divided by treatment: non-alkylating and alkylating agents.

Reference data collected from literature shows a declining trend of FD over age. FDs of non-treated cancer patients align with the reference dataset, while FDs from healthy biobank material was below reference data mean. Z-scores did not differ between cancer patients who received alkylating agents versus non-alkylating agents. Patients with Turner's syndrome had negatively deviating Z-scores, indicating lower FD compared to the reference data. To conclude, we have created a reference model of normal ovarian follicle density in human ovaries by age. This model will be a useful quality control tool in fertility preservation.