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Association between *BRCA1* promoter methylation in peripheral blood DNA and sporadic breast cancer risk in postmenopausal women

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Introduction - Breast cancer is a multifaceted disease resulting from genetic and epigenetic changes. Although pathogenic mutations in the *BRCA1* gene are thoroughly studied, the methylation of its promoter, which leads to epigenetic silencing, has also surfaced as a possible alternative mechanism that influences gene expression and tumor formation. The study aims t*o determine the association between germline BRCA1* gene promoter methylation and sporadic breast cancer.

Methods and Materials -A collection of peripheral blood DNA samples from 30 postmenopausal women diagnosed with breast cancer and 30 healthy postmenopausal women of the same age was evaluated using methylation-specific polymerase chain reaction (MSP) after the DNA was converted with bisulfite. Descriptive statistics were used to examine the relationship with clinicopathological characteristics.

Results - *BRCA1* promoter methylation was detected in 3.3% (1/30) of breast cancer patients and was absent in health controls. There was no statistically significant association between *BRCA1* promoter methylation and breast cancer risk($p=0.49$). No significant associations were found with age at menarche, parity, BMI, age at first pregnancy, breastfeeding, or contraceptive use. A significant association was observed with age at menopause($p=0.002$). Tumor characteristics, such as histological type($p<0.001$), showed a significant association with methylation status. Tumor grade, stage, lymph node involvement, and hormone receptor status [estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor 2(HER2), and triple negative breast cancer (TNBC)] did not show any associations. The only methylated case involved a grade I tumor with mixed histology.

Discussion -Germline *BRCA1* promoter methylation was found at low rate in breast cancer patients and was not detected in healthy individuals. The detection in one early-stage patient indicates a possible involvement in tumor progression; nonetheless, its rare occurrence restricts its usefulness as a predictive biomarker. Therefore, larger studies are needed to determine its relevance in risk assessment and prognosis.

Keywords - DNA Methylation, *BRCA1*, Breast Cancer, Promoter Region, Methylation Specific PCR