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GENETIC DETERMINANTS OF SPORADIC BREAST CANCER IN A COHORT OF SRI LANKAN POSTMENOPAUSAL WOMEN

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Background: While a range of common genetic variants have been shown to be associated with sporadic breast cancer risk in several Western studies, little is known about their role in South Asian populations. This study was designed to investigate the association between common genetic variants in breast cancer associated genes and the risk of breast cancer in a cohort of Sri Lankan postmenopausal women.

Methods: A case-control study involving 350 postmenopausal breast cancer patients and 350 healthy postmenopausal women was conducted. Peripheral blood DNA was genotyped using the iPLEX GOLD assay for 56 haplotype-tagging single nucleotide variants (SNV) in 36 breast cancer related genes. Odds ratios and 95% confidence intervals were obtained from adjusted logistic regression models.

Result: Four SNV [rs3218550 (XRCC2), rs6917 (PHB), rs1801516 (ATM), and rs13689 (CDH1)] were significantly associated with breast cancer risk. The rs3218550 T allele and rs6917 A allele increased the risk of breast cancer by 1.5-fold and 1.4-fold, respectively. The CTC haplotype defined by rs3218552|rs3218550|rs3218536 on chromosome 7 ($p=0.0088$) and the CA haplotype defined by rs1049620|rs6917 on chromosome 17 ($p=0.0067$) were significantly associated with increased breast cancer risk. The rs1801516 A allele and the rs13689 C allele decreased breast cancer risk by 40% and 30%, respectively.

Conclusions: These findings suggest that common genetic variants in the XRCC2, PHB, CDH1 and ATM genes, are associated with breast cancer risk among Sri Lankan postmenopausal women. The exact biological mechanisms of how these variants regulate overall breast cancer risk needs further evaluation using functional studies.