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Role of p73 polymorphism in Egyptian breast cancer patients as molecular diagnostic markers

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ABSTRACT:

Background:

The incidence of breast cancer in Egyptian women is rising; to date, a few susceptibility genes have been identified. p73 protein (also known as p53-like transcription factor or p53-related protein) is one of the ancestors of the tumor suppressor p53 protein, whose gene is located within the chromosomal loci 1p36; a region most frequently deleted in human cancers. As a consequence of sharing same domain architecture with p53; p73 might regulate p53- response genes and induced cell cycle arrest/ apoptosis in response to DNA damage. A commonly studied non-coding polymorphism consisting of a double nucleotide substitutions (G→A) and (C→T) at position 4 and 14 exon 2, situated upstream of the initial AUG regions of p73. This functional consequence of p73 polymorphism may serve as a susceptibility marker for human cancer, but the results are inconsistent.

Patients and Methods:

Eighty newly diagnosed females representing Egyptian population confirmed breast cancer patients and forty healthy controls, recruited from the departments of Experimental and Clinical Surgery and Cancer Management and Research, Medical Research Institute, Alexandria University. Single Nucleotides Polymorphism (SNP) in p73 gene (G4C14-to-A4T14) was determined in these samples by PCR-CTPP techniques.

Results:

Insignificant differences in the distributions of p73 genotypes between patients and controls were observed ($p = 0.126$). When p73 GC/GC genotype was used as the reference, the combined variant genotypes (AT/AT)/(GC/AT) was significantly associated with the risk for breast cancer [OR= 2.418, 95% CI (1.018-5.746); p= 0.042]. p73 [(GC/AT) /(AT/AT) genotypes] was found to be associated with increased risk for breast cancer among women with pathological grade III, clinical stage III, tumor size ≥ 5 cm, axillary lymph node involvement and the +ve (Her2/neu) expression, but not significantly associated with +ve ER/PR status, vascular invasion and metastasis. Furthermore, patients carrying AT variant has a favorable prognosis ($p < 0.001$) and longer survival (41.33±1.45 months) than did patients carrying GC/GC genotype (24.0±1.13 months).

Conclusion:

In conclusion, this study provides the first indication that p73 variants (AT/AT)/ (GC/AT) are risk factors for breast cancer susceptibility in Egyptian women. Thus analysis of p73 G4C14- to- A4T14 polymorphism may be useful for identifying females with higher risk to develop cancer. Additional studies are needed to confirm these findings.

Keywords:

p73, Cyclin D1, polymorphism, diagnosis, Egypt.