ROLE OF MDR1, CYP2D6 AND CCR5 GENE VARIANTS ON DRUG RESISTANCE IN BREAST CANCER PATIENTS IN QALYUBIA GOVERNORATE, EGYPT

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Abstract:
Background: Breast cancer (BC) is the most prevalent cancer affecting women worldwide. In Egyptian women, BC represents about 33.5% of all reported cancer cases. Drug resistance is an essential barrier to the success in any therapeutic approach predisposing to recurrence and death.

Objective: To investigate the distribution of multidrug resistance 1 (MDR1) C3435T, cytochrome P450 family 2, subfamily D, polypeptide 6 (CYP2D6) (*3/*4/*6) and Chemokine receptor-5 (CCR5) 32bp deletion variants and their effect on therapeutic response and progression-free survival (PFS) in Egyptian BC women.

Subjects and Methods: Forty BC patients and 20 apparent healthy controls were included. BC women were treated by surgical resection and drug therapy (FAC ± tamoxifen). Gene variations were detected by PCR amplification and reverse hybridization. Five polymorphic loci of 3 genes were covered; MDR1 C3435T, CYP2D6 (*3/*4/*6) and CCR5 32bp deletion.

Results: MDR1 C3435T polymorphism revealed significant increased frequencies of variant "T" allele, heterozygous "CT" genotype of additive model and "CT+TT" recessive model in patients versus controls. We observed increased treatment response in patients carrying at least one "T" allele. We also demonstrated significant increased frequencies of CYP2D6 *4 variant allele, CYP2D6 *4/*4 variant genotype and PM phenotype in BC patients with associated worse treatment response. The PFS for tamoxifen receiving patients, a significant difference in the rates of distant recurrence among PM versus EM was observed. The CCR5-Δ32 variant allele was completely absent in our study.

In conclusion, our study supports the role of MDR1 and CYP2D6 gene polymorphisms in BC risk and treatment response in Egyptian women from Qalyubia governorate. This association might help improve the therapeutic strategies to be patient-tailored guided by genotyping.

Key words: Breast cancer; gene polymorphism; reverse hybridization; MDR1; CYP2D6; CCR5
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