ABSTRACT

Breast cancer is one of the most common malignant tumours in Portuguese women. It's a complex and multifactorial disease where there is a strong interplay between genetic and environmental factors. In the last years, scientific researches have been trying to identify risks factors for cancer, as well as factors that will help to improve treatments.

The altered expression of some genes is a consequence for the initiation of many tumours. At present, BRCA1 and BRCA2 are the major susceptibility genes that have been identified for breast cancer however; the mutations found in these genes can only explain a small percent of all breast tumours. Experimental data suggests that estrogens can increase the risk for developing breast cancer. Since exposure to endogenous and/ or exogenous estrogens it's a risk factor, it can be considered that genetic polymorphisms that affect the expression or activity of the products of genes involved in the metabolism of estrogens and carcinogens may be a risk factor for breast cancer. We studied three polymorphisms: CYP1B1 Val^{432}Leu consisting in G to C transversion at exon 3 was reported to result in valine to leucine substitution in codon 432, the MTHFR Ala^{225}Val codes for an alanine to valine substitution in the N-terminal catalytic domain and COMT Val^{158}Met which results in a valine to methionine substitution at codon 108/ 158 of the citosolic/ membrane-bound form of the protein. We also analyzed the prevalence of 185delAG and 5382insC mutations in BRCA1 and 6174delT mutation in BRCA2.

This work is based on a case-control study, with the aim of studying whether polymorphisms CYP1B1 Val^{432}Leu, MTHFR Ala^{225}Val and COMT Val^{158} constitute a risk factor for the disease in women of Beira Interior.

We analyzed DNA samples from 62 women, of whom 30 were healthy women and 32 had breast cancer. Determinations of the genotypes corresponding to the polymorphisms and BRCA1/ BRCA2 mutations studied were performed using a PCR-RFLP based assay.

The results, for the polymorphism CYP1B1 Val^{432}Leu, suggest that women carrying the VV genotype have a higher risk for cancer breast (OR = 0.1084; 95% 0.0124-0.9466),

while women carrying VL genotype have a lower risk (OR = 8.0000; 95% 2.2197-28.8327).

The simultaneous analysis for CYP1B1 $Val^{432}Leu$, MTHFR $Ala^{225}Val$ and COMT $Val^{158}Met$ suggests that women with heterozygous genotypes have a lower risk for the disease.

The study also demonstrated that these differences appear to be more significant for pre-menopausal women.

There is imbalance of Hardy-Weinberg equilibrium for the COMT $Val^{158}Met$ polymorphism in women of Beira Interior studied.