

THE ROLE OF HLA-G POLYMORPHISM AS RISK FACTOR IN IRAQI PATIENTS WITH BREAST CANCER

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ABSTRACT : The human leukocyte antigen-G (HLA-G) is known to contribute to tumor-driven immune escape mechanisms in malignant disorders. This study aimed mainly to determine the role of IL-10 and polymorphism of HLA-G 14-bp gene as a risk factor in breast cancer (BC) patients. In this study, (50) breast cancer women and (25) healthy women as a control group were involved. Polymorphism of HLA-G 14-bp have been identified using the PCR technique. A significant elevation in the CA15-3 serum levels was observed among breast cancer patients in comparison with healthy groups (56.51 ± 4.0189 U/ml; 10.72 ± 1.48). The present results noted that elevated IL-10 level (113.0 ± 12.3 ; 44.0 ± 3.5 pg/ml) are strongly associated with breast cancer. Also, a highly significant difference was shown between breast cancer patients and the healthy control groups in homozygous genotype HLA-G 14-bp del/del genotyping (56.0% vs. 20.0%; $P < 0.01$). There was also a highly significant rise in the homozygous genotype ins/ins frequencies in patients compared to the controls (0.0%, 0.24, $P \leq 0.01$). The ins allele showed a highly significant increase in healthy control groups compared to breast cancer patients (0.52 vs 0.24, $P < 0.01$). While, a highly significant increase frequencies of del allele were demonstrated in the patient group in comparison with the controls (0.76 vs 0.48). The current results showed an association between breast cancer and HLA-G 14-bp del/del as a potential genetic risk factor in progression of the disease. While, HLA-G 14-bp ins/ins was considered as a protective factor against BC.

Key words : Gene polymorphism, IL-10, breast cancer, CEA, CA15-3.

INTRODUCTION

The most common global cancer among women is breast cancer representing about 12% of all new cancers and 25% of all women cancers (Ferlay *et al*, 2014). In breast cancer, the roles of IL-10 are controversial. IL-10 has both pro- and anti-tumor effects (Zhao *et al*, 2015). IL-10 mRNA expression is seen in more than 50% of tumor samples (Fernandez *et al*, 2005). Also more IL-10 concentrations are detected in the breast cancer patients sera than in healthy women (Khan *et al*, 2012), which is correlated with poor clinical outcome. Interleukin-10 promotes the metastasis and proliferation of tumor cells and inhibits T-cell proliferation and function (Fernandez *et al*, 2006). The human leukocyte antigen-G (HLA-G) is present in the genes of the non-classical HLA class I family of the chromosome 6p21 (Carosella *et al*, 2008). The gene of HLA-G encodes 7 isoforms via the alternative splicing of primary transcript including 4 membrane-bound and 3 soluble isoforms (Carosella *et al*, 2003). The HLA-G is found to have an essential role in immune response suppression and participates in long term immune tolerance or escape. In various disorders

such as cancers, HLA-G expression can be induced (Elliot *et al*, 2011; Tunciel *et al*, 2013). In many populations, alleles of HLA-G relatively cause restriction of polymorphism and low sequence variation (Lin *et al*, 2007; Rahimi *et al*, 2010). The HLAG protein expression is controlled by the diversity of a promoter and 3'-untranslated region (UTR) of HLA-G genes. The HLA-G genes also have the absence or presence of 14bp at the 3'-UTR (Hviid, 2006; Castelli *et al*, 2007). There is a relationship found between the splicing and stability patterns of HLA-G mRNA isoforms and the 14 bp ins/del polymorphisms in the exon 8 of the 3' UTR of HLA-G. Furthermore, HLA G polymorphisms were detected in several cancer types and regarded as predictive markers and risk factors of cancers. The objective of this study is to determine the role of IL-10 and polymorphism of HLA-G 14-bp genes as risk factors in women with breast cancer.

MATERIALS AND METHODS

This study has been performed on 50 breast cancer (Invasive ductal) women, who have been diagnosed by