

Association Serum Level Of PD-1 Receptor with Demographic, Clinical Pathological, Hormone Receptors, Molecular and Histological Subtypes in Breast Cancer Patients

Ghasaq Mohammed Muhibul¹, Eman Tariq Ali², Maitham Ali Alrikabi³

^{1,2}Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Basrah, Iraq

³Department of Clinical Pharmacy, College of Pharmacy, University of Basrah, Basrah, Iraq
Email: ghasaqmohamed1991@gmail.com

Abstract

Background: The critical role of immune checkpoints Programmed cell death receptor. Although (PD-1) has been extensively documented in a variety of malignant tumors, the basic regulatory mechanisms in breast cancer are still unclear. The objective of this study was to investigate the change in serum PD-1 concentration in pretreatment and post-treatment groups, as well as the correlation with hormone receptors, molecular and histological subtypes. **Method:** The study included 82 female breast cancer patients diagnosed before beginning treatment (pre-treatment group), 60 female breast cancer patients diagnosed after undergoing treatment (post-treatment group), and 60 healthy individuals as controls. The sPD-1 levels are measured using ELISA technique. Data on tumors were retrieved from an electronic database at the oncology centre. **Results:** The highest levels of sPD-1 were detected in the pre-treatment groups, followed by post-treatment groups compared to the healthy group. The age group (40-69 years) had the highest level of PD-1 (8.51±1.68 ng/ml) compared to other age groups. The serum level of PD-1 was significantly associated with age ($p=0.01$), family history ($p=0.0001$), and menopausal status ($p=0.04$) in the pre-treatment group. The level of PD-1 was significantly associated with the histological type of tumor ($p=0.01$), with a higher level seen in invasive tumor types. Furthermore, PD-1 levels were higher in the invasive lobular carcinoma subtype ($p=0.03$). In the post-treatment period, there was a significant association between PD-1 level and estrogen receptor status. PD-1 levels were higher in estrogen receptor-negative than in estrogen receptor-positive (1.354±0.121 vs. 0.896±0.0773 ng/ml, $P=0.01$). The higher level of sPD-1 (7.40±1.26 ng/ml) was found to be associated with the Ki-67 value (>40%) in patients with breast cancer, and the lower level of sPD-1 (5.49±1.77 ng/ml) was discovered in the Ki-67 value (<20%). Significantly, there is a positive correlation between sPD-1 level and Ki-67 expression ($p=0.004$). **Conclusion:** There was a significant association of serum PD-1 level with invasive carcinoma, particularly in invasive lobular carcinoma of patients with breast cancer, and a positive correlation with proliferation marker Ki-67 expression.

Keywords: Programmed cell death receptor (PD-1), Breast cancer, ER, PR, HER2, Histological type.

1. Introduction

The immune system in our bodies performs an essential function in protecting us from different diseases, including cancer cells [1]. Immune suppression is known to be a trademark of cancer. Various receptors and their ligands, known as checkpoints, regulate this process [2,3]. PD-1 was first described in the early 1990s as a type of immune checkpoint receptor constantly expressed on activated T cells and is inhibitory in nature by interaction with its ligands PD-L1 and PD-L2; it conserves healthy cells from excessive inflammatory or autoimmune reactions [4,5]. Even though the importance of the immune checkpoints PD-1 and PD-L1 in a variety of malignant tumors has been well established, the fundamental regulatory mechanisms in breast cancer are obscure [6]. In many countries, breast cancer is one of the most prevalent malignant tumors and the leading cause of cancer-related mortality

among women [7,8]. Multiple hereditary elements, environmental variations, and their complex interplay cause breast cancer [9,10]. Concerning cancer cells' ability to evade the immune system, the discovery of the PD-1 (programmed death 1) and PD-L1 (programmed death-ligand 1) axis has been one of the most promising discoveries in cancer therapy in latest years [11,12]. PD-1 is a highly vital component of the immune system. It is a type I transmembrane glycoprotein that belongs to the immunoglobulin CD28 superfamily [5,13]. Breast cancer treatment with anti-PD-1 therapies was efficient, especially for patients with triple-negative breast cancer (TNBC) [14]. Nivolumab is a PD-1 inhibitor that restores the anti-tumor activity of T cells by binding to PD-L1 on the surface of T cells. This blocks the immunosuppressive signaling pathway that is initiated by PDL-1/2 [4,15]. At the molecular level, breast cancer patients were classified into luminal A, luminal B, HER-2 positive, and triple negative groups according to the status of