Expression Of Cyclooxygenase-2 And Interlukin-6 Mrnas In Iraqi Patients With Breast Cancer

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Abstract

Background: Breast cancer is one of the most common malignant tumors that endanger women's health internationally, relatively uncommon in men, accounting for only 1% of all cancer cases. Location, way of life, age at marriage, and obesity are a few environmental variables that increase the risk of breast cancer.

Aim of study: the study aims to explain how the pro-inflammatory cytokines (IL-6) induce the inflammatory events in patients with breast cancer and to describe whether cyclooxygenase-2 promotes tumor growth in breast cancer or not.

Materials and methods: The current case-control cross-sectional study included 45 patients with a history of breast cancer, and it was done in multiple places in Hilla, Babylon Province, between November 2022 and March 2023.Interlukin-6 and Cyclooxygenase-2 by QPCR.

Results: The results have shown a significant increase of IL-6 ($P < 0.05$) in patients compared with control. Also, the results have shown a significant increase ($P < 0.05$) of COX2 in patients compared with control.

Conclusion: There is a significant increase in the means of Interlukin-6 and Cyclooxygenase-2 in the patients with breast cancer.

Keywords: Breast Cancer, Interlukin-6, Cyclooxygenase-2.

INTRODUCTION

Breast Cancer (BC) is one of the most common malignant tumors that endanger women's health worldwide[1]. Men's cancer is exceedingly rare, accounting for about 1% of all cancer cases[2]. It occurs when breast cells begin to proliferate uncontrollably as a result of an accumulation of essential gene changes[3]. A multitude of genetic and environmental factors contribute to such alterations and tumor growth. The lump may be asymptomatic or detectable during a physical examination of the breasts[4]. BC is a malignant tumor that starts in the breast tissue, usually in the lining of the breast lobules or milk ducts, and spreads to other parts of the body[5]. The two most common types of BC are ductal and lobular carcinoma. Ductal cancer develops in the duct to the nipple, whereas lobular cancer begins in the gland that produces breast milk[6].

Geographic location, living circumstances, age at marriage, and obesity are all environmental factors that enhance the risk of BC. Gaining weight raises the risk of having BC considerably. Gender is another major factor in BC. Furthermore, women have substantially more breast cells than men, and therefore have a significantly higher incidence risk. Another risk factor for BC is age, which raises the probability of developing the disease in older people(7).

Early detection of BC is the most effective technique for saving lives and lowering healthcare expenditures over time. BC detection and diagnosis technologies continue to advance in order to give patients with less invasive options and more accurate diagnoses(8). Cyclooxygenase-2(COX-2) is a membrane-bound and rate-limiting enzyme(9) and has long been regarded as a therapeutic center for inflammation and pain(10). The COX-2 enzyme is also known as prostaglandin (PG)-endoperoxide synthase 2 because it creates prostanoids such as prostaglandin E2 (PGE2) and helps to manage many procarcinogenic effects(11). COX-2 overexpression does, in fact, play an important role in various stages of cancer(12). Furthermore, a number of studies examining the relationship between cancer and inflammation have proposed employing COX-2 for cancer therapy or chemoprevention(12). Furthermore, epidemiological studies and clinical trials have shown that long-term use of COX-2 inhibitors like celecoxib and rofecoxib may reduce the risk of breast, lung, prostate, esophageal, liver, pancreatic, gastric, and colon cancers, as well as the Interlukin-6 (IL6) is a pleiotropic cytokine that has both pro- and anti-inflammatory actions(13). IL-6 is produced by non-cancerous cells such as monocytes, macrophages, T cells, B cells, fibroblasts, endothelial cells, and adipocytes(14). When there is an infection, inflammation, or malignancy, many distinct cell types emit IL-6(15). Intravascular angiogenesis, a critical stage in tumor formation, is stimulated by IL-6 by boosting the production of vascular endothelial growth factor (VEGF)(16). IL-6 is of particular interest because to its higher levels in BC patients' sera compared to healthy patients' sera or tissue(17).

Materials and methods:

This is a case-control cross-sectional research including 45 patients previously diagnosed with BC illness was conducted between November 2022 and March 2023 at multiple locations in Hilla, Babylon Province. Patients with BC have already been identified at the Babylon Center for Oncology. The control group is a second, often healthy group of people. The age, length of illness, smoking history, medication dose, and medical history of each patient were all determined. There were two sets of samples made, one for healthy people and one for ill people.

In this study, a quantitative reverse transcription PCR (RT-qPCR) is utilized when RNA is used as the starting material. Reverse transcriptase turns total RNA or messenger RNA (mRNA) into complementary DNA (cDNA) in this method. The cDNA is then used as a template for the qPCR procedure. RT-qPCR has applications in gene expression analysis, RNAi validation, microarray validation, pathogen detection, genetic testing, and sickness research.

Results

The current study included 45 samples from BC patients and 45 samples from healthy participants.

Clinical and demographic characteristics

The clinical demographics of the patients group were summarized in [Tab: 1] illustrated the Cyclooxygenase-2 and in [Tab: 2] for Interlukin-6 of analyzed group which was 45 patients and 45 for healthy control group. The gender distribution was only women.

According to the findings of the study, there has been a statistically significant increase in cyclooxygenase-2 levels in BC patients compared to the control group. According to the data in [Tab: 1] and [Fig: 1] it was (P 0.0).

Table1: Statistical summary of concentration of clooxegenase-2 of patients compared with control.

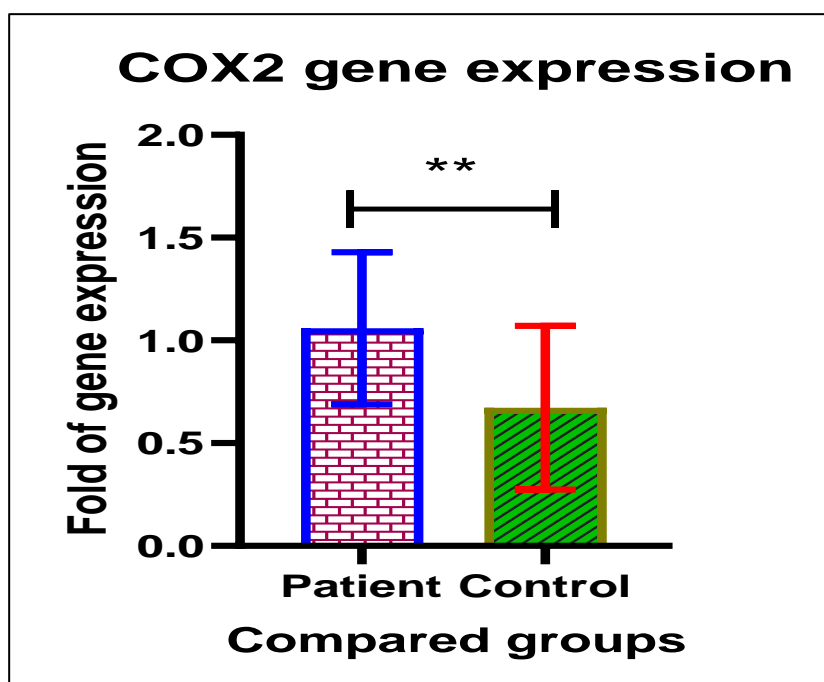| Groups	Control	Patients
Number of tested samples	24	24
mean	0.6729	1.059
Std. Deviation	0.3986	0.3702
Range	1.377	1.375
P value	0.0011	

Figure:1: The change comparison between the groups expressed COX2 gene in patient and control.

Cyclooxygenase 2 (COX-2) is an inducible form of the enzyme that catalyzes the first stage of prostanoid synthesis. Numerous studies have demonstrated that COX-2 plays an important role in the beginning and development of cancer via a number of processes, including cell proliferation, cell death, cell adhesion, and tumor neovascularization. COX-2 has also been linked to MDR via up-regulating efflux transporters (such as P-gp), which diminish intracellular drug concentration(18). Numerous studies have found that the presence of COX-2 is significantly related with large tumor size and advanced disease stage(19). The recent data reveal that COX2 levels in patients are significantly higher (P 0.01) than in controls, validating the idea that COX2 levels grow with tumor cell density. These findings are comparable to those of Basu et al. (2006), who discovered that high COX-2 levels are exclusively seen in highly invasive BC cells(20). This might explain the previously reported higher prostaglandin levels in breast tumors(21). In contrast, no COX-2 gene expression was found in normal breast tissue(22). It is unclear how COX-2 levels rise in BCs, but one possibility is that

cancer cells become intrinsically more active in COX-2 production than non-neoplastic cells(23).

Interlukin-6 was strongly associated with the group of BC patients, as shown by the fact

that their levels of the protein were much greater than those of the control group, as illustrated by the [Tab: 2] and [Fig: 2]. (P 0.01), on the other hand.

Table 2: A statistical summary of concentration of Interlukin-6 of patients compared with control.

Groups	Control	Patients
Number of tested samples	24	24
mean	0.4266	0.7049
Std. Deviation	0.2974	0.2755
Range	1.142	1.019
P value	0.7175	
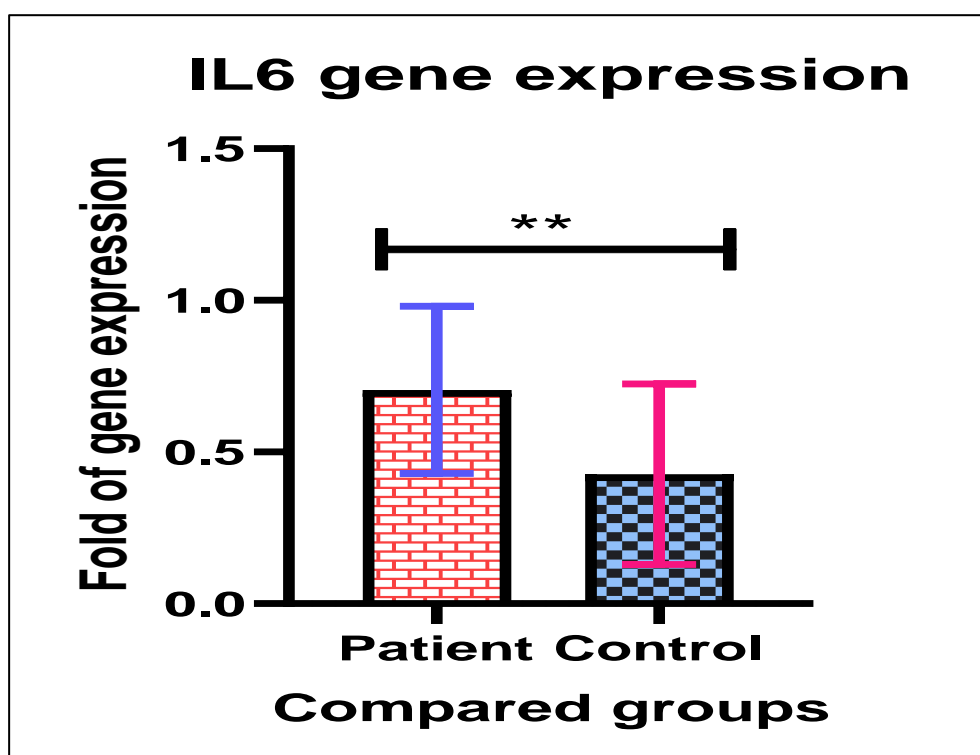
(Figure: 2): The change comparison between the groups expressed IL6 gene in patient and control.

Interleukin-6 (IL-6) is a cytokine that stimulates hematopoiesis and lymphocyte activation, but it is now being identified as a regulator of cancer formation, invasion, and metastasis. Inflammation and BC have long been associated. BC IL-6 expression increases with tumor grade, and increased blood IL-6 levels are associated with a poor prognosis for survival(24). High IL-6 levels have

previously been associated with poor overall survival and tumor growth in a range of cancers(25). Interleukin (IL)-6 may influence how cancer cells grow and disseminate, how osteolysis and humoral hypercalcemia occur, and how estrogen levels in BC tissues are managed (26). However, its specific role remains uncertain and fluctuates. It suggests that the kind of tumor cell may influence how

IL-6 promotes tumor cell growth(27). A significant upregulation of IL-6 in patients compared to controls (P 0.01) has been detected. The unregulated inflammatory responses of IL-6 cause chronic inflammation and even malignancy. BC prognosis is connected to IL-6 expression(28).

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