

Estimation of Interleukin1 Alpha and beta in serum and tissue with breast tumors patients

Wurud Ali hathal

Microbiology, College of science, University of Babylon, Wh29831@gmail.com

Frial Gemeel Abd

Microbiology, College of science, University of Babylon, frialabd@yahoo.com

Abstract

In everyday practice, breast soft tissue lesions frequently provide a diagnostic problem. They are roughly separated into malignant and benign tumor lesions, which cover a wide range of histopathological abnormalities. This study's objective is to measure the levels of IL1 and IL1 in patients with breast cancers' serum and tissue. an example of In the period from November 2021 to November 2022, breast tissue was taken from 70 female patients (aged 14 to 66) having breast surgery in Babylon Province at AL-Hilla Teaching Hospital and AL-Fayhaa National Hospital. The women underwent lumpectomies or mastectomies for benign or harmful tumors; some had a history of breast cancer, while others did not. The tissue that was gathered for analysis was combined 5 cm outside the tumor's margin in the case of females who had tumors. Fresh tissue was immediately put in a sterilized plane tube or pee cup after circumcision. It was cut, homogenized, and had a standard saline solution. and mixed with wooden sticks using a sterile surgical knife. 30 minutes after collection Using an enzyme-linked immunosorbent assay, IL1 and IL1 were evaluated in the serum and tissue of both healthy and breast tumor-bearing women (ELISA) The results showed that the mean of IL1 in serum of breast cancer was 1.052 and the mean of IL1 in Benign breast tumor was 1.208 that increased significantly in patients compared with control. Additionally, the mean of IL1 in serum of breast cancer was 5.287 and the mean of Benign breast tumor was 4.993 that did not increase significantly compared with control, and the mean of IL1 beta in locally was 21.000 increase significant than the mean of IL1.

Keywords: *breast tumors , IL1 β and IL1 α Systemic and local.*

Introduction

Breast disorders include a wide range of ailments. Most breast illnesses are not malignant. Some of these lesions required just minor treatment because they were clinically unremarkable. Nonetheless, some symptoms may have clinical significance and draw both the patient's and the treating physician's attention, particularly if they continue or worsen. (1)

Immune cells from the myeloid (monocytes, macrophages, dendritic cells) and lymphoid (T

lymphocytes and B lymphocytes) lineages can be found in normal breast tissue. Rather than the stroma and fat, immune cells are mostly found in the lobules of normal breast tissue (2). At various stages of breast carcinogenesis, cancer-associated inflammation, including cancer-intrinsic inflammation and cancer extrinsic inflammation, are present(3)(4). Usually, genetically stable cancer-initiating mutations that can be predicted for pharmaceutical treatment response or resistance result in cancer-intrinsic inflammation. (5).

The cytokine family known as interleukin-1 (IL-1) is important for both starting and controlling inflammatory and immunological responses. There are eleven members of the IL-1 family, includes receptor antagonists, pro- and anti-inflammatory cytokines (6). The type 1 IL-1 receptor (IL-1R1) binds to the two defining members of the IL-1 family, IL-1 alpha (IL-1) and IL-1 beta (IL-1), which are each encoded by a different gene and have comparable biological functions.. IL-1 or IL-1 binding to IL-1R1 induces IL-1R1 dimerization with the IL-1R accessory protein (IL-1RAcP) (7).

At steady state, IL-1 is expressed constitutively in a variety of cell types, most prominently in epithelial cells, but it is also elevated in reaction to stimuli that cause inflammation and stress. Three separate mechanisms explain how this intracellular cytokine works. First, IL-1 can go from the cytosol to the cell surface, where membrane-bound IL-1 activates IL-1R1 signaling intracellularly and paracellularly to cause local inflammatory responses. Second, IL-1 acts as an alarmin or danger-associated molecular pattern when it is released extracellularly in response to the loss of membrane integrity brought on by necrotic-type cell death (DAMP). and triggering a series of inflammatory responses.(8).

Finally, similar to transcription factors, IL-1 may execute intracellular activities by moving from the cytosol into the cell nucleus. (9) Two of IL-1's major biological functions are the induction of T helper 17 (Th17) responses and sterile and pathogen-induced inflammation (10) (11) This study sought to determine the levels of IL1 and IL1 in systemic and local tissues in people with breast cancer because TLR6 concentrations were higher raised in local (tissue) than systemic with various tumor types (21).

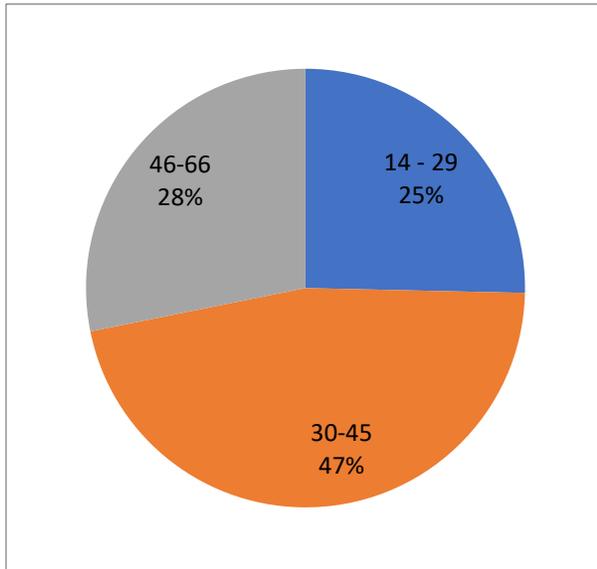
Materials and methods

Blood and breast tissue samples were collected from 70 women (aged 14 to 66) who underwent breast surgery at AL-Hilla Teaching Hospital and AL- Fayhaa National Hospital in Babylon Province between November 2021 and November 2022. Some of the women had previous breast cancer, while others did not, and all underwent lumpectomies or mastectomies for benign or malignant tumors. The tissue that was gathered for analysis was combined 5 cm outside for females who had tumors. the tumor's margin. after a circuscision, Within 30 minutes of collection, the fresh tissue was sliced and homogenized with a sterile medical knife and wooden sticks in a sterile pee cup or plane tube that was filled with a regular saline solution. Using the ELISA (Enzyme Linked-ImmunoSorbent Assays) technique, blood samples from 100 patients and 50 healthy women served as controls.which was employed in line with the manufacturer's instructions. Centrifuging was used to separate the serum, which was then utilized to test for the presence of IL1 and IL2 in the two substances.

Result and discussion

in figure (1) show that distribution of breast tumors according to age , our study show that breast tumors distributed in age (30-45) high percentage in relation to other age groupings This study contradicts study (17), which shows how menopausal status and age distributions differ between BC patients and healthy controls. did not differ significantly.

Figure (1) Distribution of breast tumors according to age



Estimation of serum level of IL-1 α and IL-1 β

Determining the immune response's contribution to breast cancer development or prevention is difficult. Despite this, a substantial body of evidence points to the possibility that the immune response in this sickness is not a host defensive mechanism and might even aid in the development of cancer. The creation of cytokines by inflammatory cell infiltrates, a direct or indirect regulator of breast cell development, is one potential mechanism for these effects (14)

In vitro studies have demonstrated that IL-1 inhibits BC cell proliferation and promotes cellular differentiation, however it is also known that IL-1 stimulates the expression of a number of proteolytic enzymes in human cancer. (19).

Table 1 showed that compared to healthy groups, BC patients had significantly higher serum IL-1 levels. This result supports study (15), which found that BC patients had significantly higher serum levels of IL-1 than control groups (median value: 19.8 pg/ml).

Also, our results support those of other writers who have found that sera from BC patients had considerably greater levels of innate cells-related cytokines (IL-1) than do sera from control groups (12) (13) According with study (15), serum IL-1 levels were considerably greater in BC patients (19.8 pg/ml, 19 pg/ml, and 46.4 pg/ml, respectively) than in BBL patients and healthy controls (5.8 pg/ml, 6.6 pg/ml, and 11.2 pg/ml, respectively). They support research demonstrating that IL-1, IL-6, and TNF- are much more prevalent in the serum of BC patients than that of control groups (16) but no discernible increase in blood IL-1 levels relative to healthy groups among BC patients. This study contradicts study (17), which found that BC patients had significantly greater serum levels of IL-1 and IL-1R1 than controls (p 0.05). IL-1 levels in breast cancer were substantially higher than in healthy individuals (median 95.45; range, 84.80-113.8) and VEGF levels in breast cancer were significantly higher than in healthy individuals (median 237.0; range, 209.5-255.6), according to study (20). (median 81.45; range, 71.20–100.2)

Table (1) The difference in median levels of serum IL-1 α (pg/ml) concentration among the Breast cancer and Healthy group

| Parameters | M \pm SD | | P_value |
|--------------|-----------------------|-----------------------|--------------------|
| | Breast cancer | Healthy | |
| IL1 α | 1.052 \pm 0.5 77 | 0.616 \pm 0.2 38 | 0.009 ** |
| IL1 β | 5.287 \pm 3.0 95 | 3.640 \pm 1.9 96 | 0.09 |

Our findings were in line with those of (15), who found that patients with benign breast cancer had significantly higher serum IL-1 levels than control group participants (median = 19.8 pg/ml). Also, our findings are consistent with those of other researchers who discovered

that sera from patients with benign breast tumors included much higher amounts of cytokines associated to innate cells (IL-1) than did sera from control groups (12). (13). Our study did not agree with study agree with study (15) show that revealed a significant elevation in serum IL 1 levels among patients with benign breast tumors (19.8 pg/ml, 19 pg/ml, and 46.4 pg/ml, respectively), in contrast to BBL patients and healthy controls (5.8 pg/ml, 6.6 pg/ml, and 11.2 pg/ml, respectively) (p0.001). According to the findings of our investigation, there was no discernible increase in serum IL-1 levels as compared to healthy groups in patients with benign breast cancers.

Table (2) The difference in median levels of serum IL-1α (pg/ml) concentration among the Benign breast tumors and Healthy group

| Parameters | M±SD | | P_ value |
|------------|----------------------|-----------------|----------------------------|
| | Benign breast tumors | Healthy | |
| IL1 α | 1.208±0.5 89 | 0.616±0.2 39 | 0.000* ** |
| IL1β | 4.993±3.5 90 | 3.640±1.9 96 | 0.2 |

Estimation of mucosal level of IL-1α and IL-1β

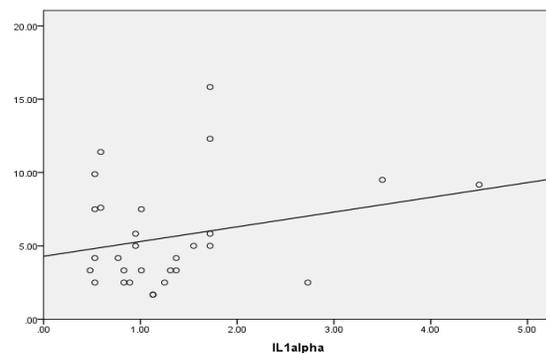
Our study did not agree with study agree with study (15) show that revealed a significant elevation in serum IL 1 levels among patients with benign breast tumors (19.8 pg/ml, 19 pg/ml, and 46.4 pg/ml, respectively), in contrast to BBL patients and healthy controls (5.8 pg/ml, 6.6 pg/ml, and 11.2 pg/ml, respectively) (p0.001). According to the findings of our investigation, there was no discernible increase in serum IL-1 levels as compared to healthy groups in patients with benign breast cancers.

Table (3) The difference in median levels of serum and mucosal IL-1α and IL-1β (pg/ml) concentration among patients with breast tumors

| Parameters | M±SD | | P- value |
|------------|-----------------|-------------------|----------|
| | Blood | Tissue | |
| IL1 beta | 5.599±3.5 50 | 21.000±14. 356 | 0.001** |
| IL1 alpha | 1.304±0.9 13 | 1.086±0.81 8 | o.4 |

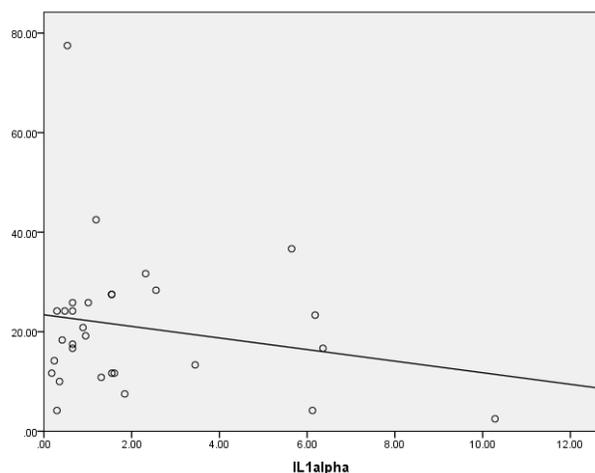
In figure (2) show that Correlation between IL1β and IL1α in blood was positive correlation and no significant with P= value = 0.1 and correlation value was = 0.3

Figure (2) correlation between IL1α and IL1β in blood



In figure (3) correlation between IL1 α and IL1β in locally was no significant with P- value = 0.3 and negative correlation with value p= - 0.2

Figure (3) correlation between IL1 α and IL1 β locall



Conclusion

Study disease distribution in age groups 30-45 more than other age groups due to population differences; the concentration of IL1 in serum of BC and BBT was higher significantly compared with control; however, IL1 in serum of BC and BBT was not increased significantly compared with control; in local the IL1 in tissue was increased significantly compared with blood; however, IL1 was not significantly different in the concentration in blood and local; the correlation between IL1 and IL1 wa

Acknowledgements

We are grateful to Dr. Wala Noori Majeed Baram for assisting us obtain breast tissue.

Reference

Alamri,A.M., Alsareii1,S.A., Al-Wadei1,H.H., Al-Qahtani,A.M., Sultan,S.A.A., Alshamrani ,S.A., Almakrami , A.H., Dael,A.A., Alyami ,A.Y., Hommadi,A.M., Ali ,Y.A.T. (2020).Epidemiological Pattern of Breast Diseases among Females in the South-Western Region, Saudi Arabia

International Journal of Clinical Medicine, 2020, 11, 257-269.

Degnim AC, Brahmhbhatt RD, Radisky DC, et al. Immune cell quantitation in normal breast tissue lobules with and without lobulitis. *Breast Cancer Res Treat.* 2014;144:539–549.

Lim ,B., Woodward ,W.A., Wang ,X., Reuben ,J.M., Ueno ,N.T.(2018). Inflammatory Breast Cancer Biology: The Tumour Microenvironment is Key. *Nat Rev Cancer* . 18(8):485–99

Comen ,E.A., Bowman ,R.L., Kleppe ,M.(2018). Underlying Causes and Therapeutic Targeting of the Inflammatory Tumor Microenvironment. *Front Cell Dev Biol* (,6:56.

Todoric ,J., Antonucci ,L., Karin ,M. (2016) . Targeting Inflammation in Cancer Prevention and Therapy. *Cancer Prev Res (Phila)* . 9(12):895–905..

Garlanda, C ., Dinarello , CA ., Mantovani , A.(2013) The interleukin-1 family: back to the future . *Immunity* . 39(6) 1003 – 1018

Verstrepen, L.; Bekaert, T.; Chau, T.-L.; Tavernier, J.; Chariot, A.; Beyaert, R.(2008). TLR-4, IL-1R and TNF-R signaling to NF-kappaB: Variations on a common theme. *Cell. Mol. Life Sci*, 65, 2964–2978.

Cohen ,I .,Rider ,P., Carmi ,Y., et al.(2010). Differential release of chromatin-bound IL-1alpha discriminates between necrotic and apoptotic cell death by the ability to induce sterile inflammation , *Proc Natl Acad Sci USA* . 107(6) 2574-2579

Netea , M.G., van de Veerdonk ,F.L., van der Meer, J.W., Dinarello ,C.A., Joosten, L.A.(2015). Inflammasome-independent regulation of IL-1-family cytokines . *Annu Rev Immunol.* 33,49-77

- Garlanda, C., Dinarello, C.A., Mantovani, A. (2013) The interleukin-1 family: back to the future. *Immunity*. 39(6) 1003 – 1018
- Chung, Y., Chang, S.H., Martinez, G.J., et al. (2009). Critical regulation of early Th17 cell differentiation by interleukin-1 signaling *Immunity*. 30(4). 576 – 587
- Sheen-Chen S-M, Chen W-J, Eng H-L, Chou F-F. Serum concentration of tumor necrosis factor in patients with breast cancer. *Breast Cancer Res Treat* 1997; 43:211-215.
- Fuksiewicz M, Kaminska J, Kotowicz B, Kowalska M, Rubach M, Pienkowski T. Serum cytokine levels and the expression of estrogen and progesterone receptors in breast cancer patients. *Clin Chem Lab Med* 2006; 44(9):1092-7.
- Stewart TH, Heppner GH. Immunological enhancement of BC. *Parasitology*, 115 suppl 1997; S 141-S153.
- Ahmed A .Al-Hassan, Nidhal Abdul Muhymen, Ala'a Ghany Hussien FICMS, Leen K. Mustafa 3 FICMS, Eman Sh. Al-Obeidy. (2010). *IRAQI J MED SCI*, 2010; VOL.8 (1):11-17
- Singer CF, Kronsteiner N, Hudelist G, Marton E, Walter I, Kubista M, Czerwenka K, Schreiber M, Seifert M, Kubista E. Interleukin 1 system and sex steroid receptor expression in human breast cancer: interleukin 1alpha protein secretion is correlated with malignant phenotype. *Clin Cancer Res*. 2003 Oct 15;9(13):4877-83. PMID: 14581361.
- Wang J, Shi Y, Wang G, Dong S, Yang D, Zuo X. The association between interleukin - 1 polymorphisms and their protein expression in Chinese Han patients with breast cancer. *Mol Genet Genomic Med*. 2019;7:e804
- Bel'skaya, L.V.; Loginova, A.I.; Sarf, E.A. Pro-Inflammatory and Anti-Inflammatory Salivary Cytokines in Breast Cancer: Relationship with Clinicopathological Characteristics of the Tumor. *Curr. Issues Mol. Biol*. 2022, 44, 4676–4691.
- Bourhis XL, Toillon RA, Boilly B, Hondermarck H. Autocrine and paracrine growth inhibitors of breast cancer cells. *Breast Cancer Res Treat*. 2000 Apr;60(3):251-8. doi: 10.1023/a:1006461621905. PMID: 10930113.
- Mohammed, T.F. and Qadir Saudi, F.A. (2023). *Journal of Biological Sciences* 30 (2023) 103544
- Shather, T. S., & Abd, F. G. (2022). Survey the bacterial types in breast tissue and CA13-5 for women with breast disease in Babylon province. *International Journal of Health Sciences*, 6(S4), 6198–6208.