Correlation of the Interlukein-8 with Breast Cancer Patients in Iraqi Woman's

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Abstract

Almost one-third of all female malignancies recorded in Iraq's most recent Iraqi Cancer Registry are breast cancers, making it the most common kind among women. With an anticipated 9.6 million deaths due to cancer in 2018, it is the second largest cause of death worldwide. One out of every six people who die in the world does so as a result of cancer. In low- and middle-income nations, cancer kills more than 70 percent of the population. Methods: This study include 49 samples patients and 40 samples (control group) which collection by draw of blood by gel tube and also the specimens were used centrifuge to get serum to measuring the interlukein-8 level by ELISA technique to both groups (patients, control). Results: measured IL-8 levels by ELISA technique and the results were referred to raise in IL-8 levels of BC females for serum samples compared with control group (healthy women). The cutoff value of serum IL-8 was >26.73 with good sensitivity, specificity and accuracy level respectively (73.47 %, 75 % and 72.0 %). The serum level of IL-8 was significantly higher in breast cancer group in comparison with control group, 36.69 (27.39) fold change versus 20.55 (13.83) fold change, respectively (p < 0.001). Conclusion: This study has found that the investigated interlukein-8 levels were associated with moderate to high grade carcinoma, this study may clarify that IL-8 along very important predictive and diagnostic marker for breast cancer and treatment responsiveness.

Keywords: Interlukein-8, Breast Cancer, Biomarker, Correlation, Interleukin.

INTRODUCTION

Cancer Registry 2013 and Ministry of Health, Iraq 2017. According to the most recent Iraqi, accounting for nearly a third of all female cancer cases. (Alwan, 2016). According to a 2018 estimate, Cancer killed an estimated 9.6 million people around the globe in 2013. One out of every six people who die in the world does so as a result of cancer. (Geetha et al.2017; WHO, 2018).

Local studies in Iraq have shown that the short survival of affected individuals is primarily due to the project was in its later stages when it was shown as a result of late diagnosis and treatment (Alwan, 2016; Alwan et al.,2017). Despite the fact that After a nationwide breast cancer screening program was established in Iraq in 2001, ignorance and indifference to breast cancer as a disease has been demonstrated even among the educated population (Javeth et al.,2017).

Breast cancer diagnosis in women poses considerable challenges for early detection, correct staging, and breast cancer surveillance (Ng et al., 2013). As a result, a cost-effective and accurate screening strategy for this malignancy is still needed, as is the discovery of novel biomarkers to improve diagnosis, prognosis, and prediction (Edwin et al., 2019). According to the American Cancer Society (2012), the purpose of early breast cancer detection screening is to locate the cancer before it causes symptoms. Screening is a method of detecting an illness in people who have no symptoms, such as cancer. Early detection refers to a method that allows breast cancer to be detected earlier than it would have been otherwise (Ravindra et al., ; Ng et al., 2013).

An autocrine or paracrine chemokine, Interleukin-8 (IL-8) has a tumor-promoting effect and is a promising biomarker for cancer prognosis and prediction. (Patidar et al., 2012; Todorović and Milovanović, 2013). ER and ER+ breast cancer cells benefit from IL-8's ability to invade and spread. Breast tumors that are HER2-positive have an elevated level of this protein as well. The blood of cancer patients contains higher concentrations of it as well. (Sampoornam, 2014).

MATERIALS AND METHODS

Study design and samples collection: The study, involved 49 Patients' samples were obtained, particularly women with breast cancer, during period from October 2021 to April 2022 and blood samples (gel tube) were fully taken with serum samples, in addition to taking samples in the same way as combining those healthy women (control group) 40 samples.

The study includes take information's patient (age, city, family history, number of children and to adding information from histopathology examination). Data were gathered from first-degree relatives in several cases.

Also using serum samples in gel tubes to measure the level of interleukin 8 compared to the samples of healthy women in the Elisa technique.

Measurement of Human IL-8 (Interleukin 8) by ELISA

IL-8 is a human protein (Interleukin 8) For the quantitative determination of IL-8 concentrations in serum samples, ELISA was utilized as described below by the manufacturer (Elabscience).

Calculation, in the form of a final result:

The optical density readings for each standard and sample were used to determine the ELISA results. OD values for each standard were then plotted A best fit curve was created through the data points, with concentration on the X-axis and time on the Y-axis.that show in figure(1)
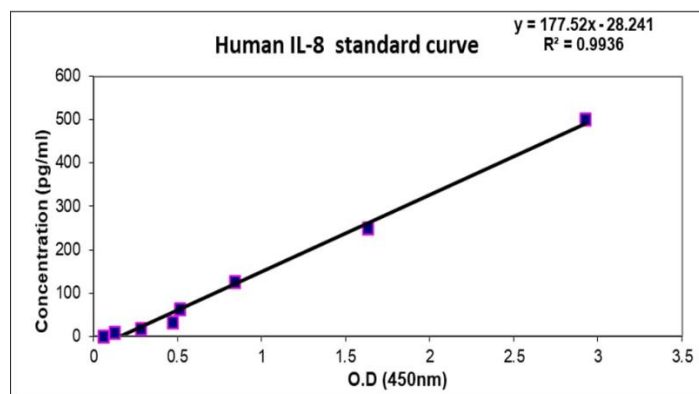

Figure (1) show IL-8 standard curve

Table (1) show Dilutions chain that used in Elisa kit to determination IL-8 level to explained truth results that discovered color change after used substrate reagent in all wells.

Standard	Mean O.D	Concentration (pg/ml)
ST.1	2.925	500
ST.2	1.631	250
ST.3	0.841	125
ST.4	0.517	62.5
ST.5	0.473	31.25
ST.6	0.285	15.63
ST.7	0.128	7.81
ST.8	0.062	0

RESULTS

A comparison of the average age of those with and without breast cancer.

Breast cancer group and control group mean age is compared in the table (2). Patients with breast cancer ranged in age from 37 to 80 years old, with an average age of 52.33 years and an average age difference of 8.31 years. There was a wide range of ages in the control group, ranging from 32 to 61 years old. Mean age differences between patients and controls were found to be insignificant can't (p = 0.073).

Table (2) show mean age.

Characteristic	Breast cancer group n = 49	Control group n = 40	p
Age (years)			
Mean ±SD	52.33 ±8.31	49.33 ±7.01	0.073 I NS
Range	37 -80	32 -61	
30-39, n (%)	5 (10.2 %)	3 (7.5 %)	
40-49, n (%)	12 (24.5 %)	14 (35.0 %)	
50-59, n (%)	20 (40.8 %)	20 (50.0 %)	
60-69, n (%)	11 (22.4 %)	3 (7.5 %)	
70-80, n (%)	1 (2.0 %)	0 (0.0 %)	

It is important to note that the number of cases, standard deviation, and t-test are all used in this experiment.

Measuring serum IL-8 in patients with breast cancer and control group

IL-8 levels in the blood were markedly elevated in breast cancer group in comparison with, control group, 36.69 (27.39) fold change versus 20.55 (13.83) fold change, respectively (p < 0.001) in table (3), as shown in figure 2.

Table (3) The gene expression of serum IL-8 in patients with breast cancer and control group

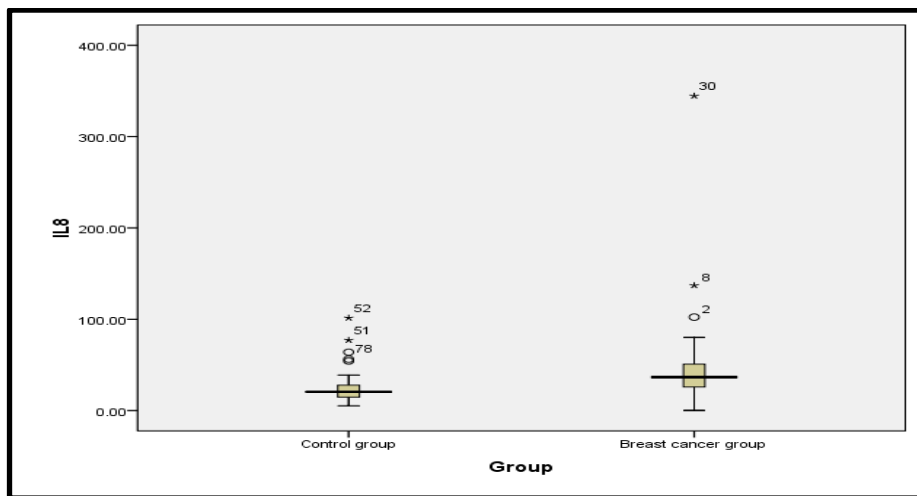| Characteristic	Breast cancer group n = 49	Control group n = 40	P
IL-8			
Median (IQR)	36.69 (27.39)	20.55 (13.83)	< 0.001 M **
Range	0.17 -344.57	5.15 -101.44	

Figure 2: Box plot showing Breast cancer patients have elevated levels of IL-8. and healthy controls

The serum, IL-8 of cutoff value was >26.73 with good sensitivity (73.47 %), good specificity (75 %) and good accuracy level (72.0 %).

Table (4) The ROC characteristics

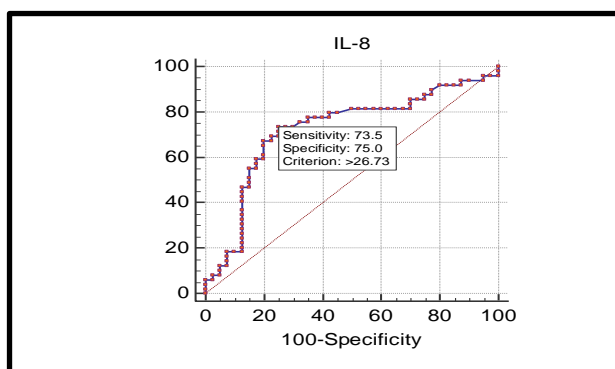| Characteristic	IL-8
Cutoff	>26.73
AUC	0.721
95% CI	0.616 to 0.811
P-value	< 0.001
Sensitivity %	73.47
Specificity %	75
Accuracy %	72.1

Figure 3: Receiver operator characteristic curve (ROC) analysis to determine a cutoff value for breast cancer diagnosis of IL-8.

DISCUSSION

The lack of in this type of case control study, a considerable age gap between the paints and the control group is required in order to eliminate any bias in the results that might be caused by significant variation in mean age. In our study, the mean age was 52.33 ±8.31 years with a range of 37 to 80 years and this mean is nearly similar to another Iraqi study done in Basra in which the The average patient was 50 years old when they were first diagnosed (range 22-85 years) (Abood, 2018) and this study included 1,128 patients with breast cancer. According to (Dabakuyo-Yonli, and Arveux, 2020), the average age at diagnosis is 63 years old and this study was done France which revealed that average age of women diagnosed with breast cancer in France is higher than that in our study.

Arabian patients are said to show up with breast cancer a decade earlier than those in the Western world, according to one study (Albeshan et al., 2018). At diagnosis, our study found that the average age of participants was 50 years old, which is in line with findings from Arab studies. such as Yemen (El-Zaemey et al., 2012), Bahrain (Hamadeh et al., 2014), Jordan (Sampoornam , 2015), (Mehdi et al., 2014), and Lebanon (Arkoob et al., 2014). (Mehdi et al., 2014). Chahine and coworkers (2015) As a result, in the United States and Western Europe, average age of breast cancer patient's diagnosis is significantly older than in other countries (Seela et al., 2015). Iraqi and neighboring region's women are more likely than those in the United States and Western Europe to acquire breast cancer at a younger age. As a result, it is critical to construct screening programs for Iraqi women in their early adulthood, while research into age-specific incidence rates is needed to establish a high risk at an earlier age.

In a recent Iraqi study done in Erbil, 55 patients with breast cancer were compared to 40 control subjects and the results showed that the level of serum IL-8 in breast cancer was higher than that of control group (Azeez and Rafiq, 2021) and therefore we agree with them in that serum IL-8 is a possible marker for breast cancer aiding in diagnosis and prognosis. However, the level in (Azeez and Rafiq, 2021) study was 101.55 which is higher than our level (36.69) and this low level in our study can be explained because patients received chemotherapy and it has been shown in a recent study that the administration of chemotherapy will cause reduction in the serum level of IL-8 and this is considered as a marker of response to chemotherapy (Tiainen et al., 2019).

In a Chinese study (Wang and Yang, 2017) which enrolled 534 breast cancer patients and 452 matched healthy individuals, they found that serum IL-8 of compared to healthy controls, the number of cases was considerably greater. Thus, we agree with (Wang and Yang, 2017) in that serum IL-8 increases in breast cancer.

Yoshimura identified IL-8, a cytokine with pro-tumorigenic and pro-angiogenic properties that plays a role in inflammation and immunology (Lakshmi et al., 2019). It has been observed that IL-8 and its receptors are overexpressed in a wide range of cancer cells. Studying primary breast cancer tissues, researchers found that Angiogenesis has been linked to the cytokine IL-8. which is necessary for the development and spread of the tumor. In addition, increased cancer cell proliferation has been associated to IL-8 (Padmaja et al., 2020).   An increased TNM staging and the involvement of IL-8 in cancer progression have been associated to hormone receptor-positive lymph nodes. In this investigation, IL-8 It has been demonstrated that expression is considerably higher in experimental group than in the healthy controls. In patients who had a positive response to treatment, levels of IL-8 were lower than they were at baseline. It is hoped that IL-8 can be used to predict the prognosis and identify genes and proteins that are considered differently in patients with breast cancer (Wang and Yang, 2017).

CONCLUSION:

This study has found that the investigated interlukein-8 levels were associated with moderate to high grade carcinoma. This study may clarify that IL-8 very important predictive and diagnostic marker for breast cancer and treatment responsiveness.

DATA AVAILABLE STATEMENT:" The datasets used and/or analyzed during the current study will be available from the corresponding author on reasonable request."

REFERENCES

1. Abood R. A. Breast Cancer in Basra Oncology Center: A Clinico- Epidemiological Analysis. Asian Pacific journal of cancer prevention APJCP, 2018, 19(10),2943–2946. https://doi.org/10.22034/APJCP.2018.19.10.2943.
2. Albeshan SM, Mackey MG, Hossain SZ, Alfuraih AA, Brennan PC. Breast cancer epidemiology in Gulf cooperation council countries: A regional and international comparison. Clin Breast Cancer. 2018 ;18: e381–92.
3. Alwan NAS. Breast Cancer Among Iraqi Women: Preliminary Findings from a Regional Comparative Breast Cancer Research Project. J Glob Oncol. Mar, 2016 ; 16;2(5):255-258. 2017.
4. Alwan, N., Mualla, F. H., Al Naqash, M., Kathum, S., Tawfiq, F. N., & Nadhir, S. Clinical and Pathological Characteristics of Triple Positive Breast Cancer among Iraqi Patients. The Gulf journal of oncology, 2017; 1(25), 51–60.
5. Alwan, Nada AS. "Breast cancer among Iraqi women: Preliminary findings from a regional comparative Breast Cancer Research Project." Journal of Global Oncology, 2016; Vol. 2, No. 5, pp. 255-58.
6. American Cancer Society . Cancer Prevention and early detection Facts and Figures, 2012,
7. Arjun Patidar, S.C.Shivhare, Umesh Ateneriya, Sonu Choudhary. A Comprehensive Review on Breast Cancer. Asian J. Nur. Edu. & Research 2(1): Jan.-March 2012; Page 28-32.
8. Athar Javeth , R. G. Mathur, Molly Babu. A correlational survey to assess the level of stress, coping strategies, and quality of life of female cancer patients related to chemotherapy induced alopecia in Amala Cancer Hospital, Thrissur, Kerala. Asian J. Nur. Edu. and Research.2017; 7(1): 1-6.
9. Azeez SH, Rafiq SN. Immunological Status in breast Cancer Women's in Erbil Province-Iraq. P J M H S, 2021; 13 (3), 1629-1634.
10. B. Edwin Jose, P. Muralidharan. Effect of Azima tetracantha Lam on Human Breast Cancer Cells MCF-7. Research J. Science and Tech. 2019; 11(2):109-112.
11. Bhagya Seela S, Shanmuga Raju P, Ezhilarasi R. Role of Nursing in Lymphoedema with Breast Cancer Patients. Asian J. Nur. Edu. and Research 5(4): Oct.- Dec.2015; Page 542-544.
12. Chahine G, El Rassy E, Khazzaka A, et al. Characteristics of incident female breast cancer in Lebanon 1990-2013: Descriptive study of 612 cases from a hospital tumor registry. Cancer Epidemiol. 2015 ; 39:303–6.
13. Dabakuyo-Yonli, S., & Arveux, P. Épidémiologie du cancer du sein [Epidemiology of breast cancer]. La Revue du praticien, 2020; 70(7), 726–729.
14. El-Zaemey S, Nagi N, Fritschi L, Heyworth J. Breast cancer among Yemeni women using the National Oncology Centre Registry 2004-2010. Cancer Epidemiol. 2012; 36:249–53.
15. Hamadeh RR, Abulfatih NM, Fekri MA, Al-Mehza HE . Epidemiology of breast cancer among Bahraini women: Data from the Bahrain Cancer Registry. Sultan Qaboos Univ Med J. 2014 ; 14:176–82.
16. Lakshmi K. M.1, Jaseela K. T., Anjana P, Ayisha Sithara M. T. Dhrishya. Assess the awareness regarding Early Identification, Prevention and Management of Breast Cancer among Early Adult Women. Asian J. Nursing Education and Research. 2019; 9(1):04-08.
17. M. Geetha, K. Menaka, P. Padmavathi. Awareness of Breast self-examination and risk factors of Breast Cancer among Women. Asian J. Nur. Edu. and Research.2017; 7(3): 413-416.
18. Mehdi I, Monem EA, Al Bahrani BJ, et al. Age at diagnosis of female breast cancer in Oman: Issues and implications. South Asian J Cancer. 2014 ;3:101–6.
19. Ng, E.; Rufina, L.; Vivian, Y.; Hong, C. and Candy, P. Circulating miRNAs as specific biomarker for breast cancer detection. PLoS One, 2013 ; 8: e53141.
20. Padmaja A, Mohanasundari S K, Munuswamy, Murali, K. Sesha Kumar. Evaluate The effectiveness of Awareness programme with health Education on breast cancer and skill Training on breast self-Examination among rural women in chittoor Dist Andhra Pradesh-A Collaborative Research. Asian J. Nursing Education and Research. 2020; 10(1):97-102.
21. Ravindra B. Saudagar, Nachiket S. Dighe, Deepak S. Musmade , Vinayak M. Gaware, D. A. Jain. SERM's in Treatment of Breast Cancer. Asian J. Pharm. Res. 1(4): Oct. - Dec. 2011; Page 81-86.
22. Sampoornam. W. Hermeneutic circle focusing lived experience of Breast Cancer Survivorship- A Phenomenological Approach. Asian J. Nur. Edu. and Research 5(3): July- Sept.2015; Page 439-442.
23. Sampoornam. W. Stress and Quality of Life among Breast Cancer Patients. Asian J. Nur. Edu. & Research 4(3): July- Sept., 2014; Page 325-327.
24. Tiainen L, Hamalainen M, Luukkaala T, Tanner M, Lahdenpera O, Vihinen P, et al. Low plasma IL-8 levels during chemotherapy are predictive of excellent long-term survival in metastatic breast Cancer. Clin Breast Cancer. 2019.
25. Todorovic-Rakovic N, Milovanovic J. Interleukin-8 in breast cancer progression. J Interferon Cytokine Res. 2013;33(10):563–70. doi: 10.1089/jir.0023. [PubMed: 23697558].
26. Wang, H., & Yang, X. Association between serum cytokines and progression of breast cancer in Chinese population. Medicine, 2017; 96(49), e8840. https://doi.org/10.1097/MD.0000000000008840.
27. World Health Organization. Indicators for assessing infant and young child feeding practices. Washington D.C., U.S.A: World Health Organization (2018).