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Correlation Between P53 and Interleukins (IL-2, IL-8) and Their Role in Breast Cancer

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ABSTRACT

Background: P53 is a crucial tumor suppressor gene involved in maintaining genomic stability. This study aimed to examine the correlation between P53 expression and interleukins (IL-2 and IL-8) in breast cancer patients and to evaluate their potential as biomarkers.

Methods: Blood samples were collected from 40 breast cancer patients and 20 healthy controls. Quantitative real-time polymerase chain reaction (RT-PCR) was used to assess P53 expression, while enzyme-linked immunosorbent assay (ELISA) measured IL-2, IL-8, and P53 titers. Statistical analysis was performed using SPSS.

Results: breast cancer patients exhibited significantly higher IL-2 (10.6±3.2 pg/mL, P=0.003) and IL-8 (25.7±4.5 pg/mL, P=0.001) levels compared to controls. In contrast, P53 titers were lower in breast cancer patients (129.7±55.9 pg/mL) than in controls (175.6±233.8 pg/mL, P=0.02). A weak positive correlation was found between IL-2 and P53 (r=0.01), while IL-8 had a weak negative correlation with P53 (r=−0.02). RT-PCR analysis of 15 selected patients revealed a significant reduction in P53 expression (P=0.002) compared to controls.

Conclusion: The study suggests that increased IL-2 and IL-8 levels, along with decreased P53 expression, may contribute to breast cancer progression. These cytokines could serve as potential biomarkers for prognosis and diagnosis. However, limitations include a small sample size, lack of clinical data, and weak correlations, requiring further studies with larger cohorts and comprehensive clinical profiling.

INTRODUCTION

Breast cancer is the most frequently diagnosed malignant tumor in women and the leading cause of cancer-related death worldwide. Globally, the prevalence of breast cancer is steadily rising.[1] In Iraq, breast cancer is considered the leading cancer among Iraqi women.[2] The immune system is shielded from cancer initiation through cancer immunity. The humoral immune system (B lymphocytes) and cellular immune system (T lymphocytes) are 2 defense mechanisms against cancer cells. Cellular immunity is crucial, even though it works against tumor cells. T-helper type 1 (T_H1) cells produce the lymphokine interleukin-2 (IL-2).[3]

The chemokine IL-8 has major potential as a prognostic and predictive biomarker of cancer. It plays an autocrine and paracrine role in tumor generation. IL-8 may serve a special function in breast cancer, primarily driven by the expression of human epidermal growth factor receptor 2 (HER2) and estrogen receptor (ER).[4] Both malignant and stromal cells generate interleukin-8, which is released in response to endothelial cells and monocytes. Previous research has indicated that IL-8 promotes cell invasion, metastasis, and angiogenesis, accelerating the growth of breast cancer cells.[5]

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Immunology and cancer virus research have led to a strong interest in research on p53. Immunotherapy is now the mainstay of cancer treatment, and numerous indications point to the function of the p53 protein as an antigen in adaptive immune responses as well as in the control of the innate immune system. As a component of the innate immune system, the p53 gene and protein are crucial for the surveillance of repetitive DNA and RNAs, senescence, aging, and infectious illnesses. In cancers, a mutant form of the p53 protein triggers both a tumor antigen (B-cell antibody response) and tumor-specific transplantation antigen (CD-8 killer T-cell response).[6]

The main function of the p53 protein is tumor suppression. TP53 is responsible for protein expression and is found on the human chromosome 17. It has been suggested that p53 prevents genomic and phenotypic changes associated with the onset of cancer. This is because of the intricate connections across several signaling pathways that are essential for fundamental biological functions.[7] When specific DNA response factors or elements are bound to the wild-type p53 protein, a wide variety of genes are expressed. This results in protection against the onset and spread of cancer.[8-10]

A *TP53* gene mutation has been found in almost half of human breast cancer cases. In the event of DNA damage, wild-type p53 inhibits cell reproduction until the damage is fixed. Consequently, the spread of cells with faulty DNA ceases.[11-13] TP53 mutations affect the cell cycle. These mutations result in loss of cellular regulation during cell division. This causes faulty DNA to pass to the progeny, and, consequently, malignant cells arise.[14] These transcription factors play critical roles in coordinating several cellular reactions. These reactions include cell cycle arrest, differentiation, DNA repair, senescence, cell death, and metabolism. This results in the activation of the biological mechanisms that suppress cancer progression. The "guardian of the genome" is one such response, as genomic integrity is maintained.[15] A review of the literature on the correlation between P53 and some interleukins and their role in breast cancer shows the scarcity of research in Iraq. Thus, this study was designed to investigate the expression of the p53 gene in breast cancer patients, immune parameter levels, and the correlation between them.

METHODS

Sample collection

Forty blood samples were obtained from breast cancer patients at the Emergency Center of Medical City Hospitals in Baghdad, and 20 samples were obtained from healthy people between January 2024 and March 2024. The patients' ages ranged from 35 to 76 years.

Each patient provided 5 mL of blood, which was divided into 2 mL in a gel tube without an anticoagulant and allowed to clot at room temperature. The blood was then centrifuged at 2000*g* for 10 minutes. Serum samples were kept at −20 °C until use for enzyme-linked immunosorbent assay (ELISA), and 3 mL was kept in an ethylenediaminetetraacetic acid (EDTA) tube with anticoagulant at −20 °C for RNA extraction.

Inclusion and exclusion criteria

The inclusion criteria included age of more than 18 years with histologically proven breast cancer and willingness to be enrolled in the p53 genetic study. Exclusion criteria included dual malignancy and male breast cancer.

Inclusion of Primer Sequences

The sequences, their respective locations within the gene, and the NCBI accession number (NM_000546.6) are provided below in Table 1.

Table 1. The Primer Sequences Used in This Study for the *TP53* Gene

Gene	Primer	Sequence (5'→3')	Location within sequence (Nucleotide)	Reference
TP53	Forward	5'-AGCTTTGAGGTGCGTGTTT-3'	701–720	NM_000546.6
TP53	Reverse	5'-CTGTTCCGTCCCAGTAGAT-3'	851–870	NM_000546.6

Gene Reference and Primer Location

The primers were designed to target specific regions of the TP53 gene, as indicated by their nucleotide positions within the reference sequence (NM_000546.6). These regions were selected based on their relevance to the gene's expression and its role in breast cancer pathogenesis.

Immunological assay

IL-2, IL-8, and P53 were analyzed using ELISA (SUNLONG, China) according to the kit instructions.

RNA extraction by TRIzol

RNA Extraction

The TRIzol 0.6 mL was used to suspend the blood, then a 15-minute incubation period was allowed to ensure complete dissociation of the nucleoprotein complex. For lysis, 200 µL of TRIzol reagent was added, along with chloroform. Then, the mixture was incubated at room temperature for 2 to 3 minutes. Later, the sample was centrifuged at 10 000 rpm for 10 minutes. Then, the mixture was separated into an upper colorless aqueous phase and a lower red

phenol-chloroform interphase as a result of this centrifugation. Subsequently, the RNA-containing aqueous phase was poured into a fresh tube. In order to precipitate the RNA, 200µL of isopropanol or absolute ethanol was added to the aqueous phase, followed by incubation at room temperature for 2 minutes. Then, the mixture was centrifuged again at 10 000 rpm for 10 minutes, resulting in the precipitation of total RNA on the filter of the spin column tube. Later, the supernatant was discarded, and 0.5 mL of washing buffer 1 was added to the column to resuspend it. Then, the tube was centrifuged for 2 minutes at 10 000 rpm, and the supernatant was discarded. After that, 0.5 mL of washing buffer 2 was added to the column to resuspend it, and the tube was also centrifuged for 2 minutes at 10 000 rpm. Then, the supernatant was discarded, and the column was preheated with 75µL of elution solution and centrifuged for 1 minute at 10 000 rpm. Lastly, the total RNA samples were stored in a deep freezer.

Amplification of specific gene cDNA Synthesis

The cDNA was synthesized using the cDNA ready-to-use kit provided by Bioneer, Korea.

In this process, 18 µL of RNA extract was added to a microfuge tube. Two µL of either hexamer primer (for prokaryotic cells) or oligo(dT) (for eukaryotic cells) were added and thoroughly mixed. The resulting mixture was then incubated in a polymerase chain reaction (PCR) machine under specific conditions: 37 °C for 10 minutes, followed by 42 °C for 1 hour, and finally 95 °C for 5 to 10 minutes in a single cycle. The synthesized cDNA was either immediately utilized as a template for qRT-PCR or stored for long-term preservation at −20 °C.

Quantitative reverse transcription-PCR (qRT-PCR)

The real-time PCR amplification was done by adding 2 µL of cDNA to the PCR tube. Then, 1 µL of each primer was added. Later, the volume was completed to 20 µL with DNase-free distilled water. Then, the mixture was mixed well and put in the qPCR machine (Table 2).

Table 2. Polymerase Chain Reaction Condition

Step	Temperature (°C)	Duration	Cycles
Initial Denaturation	95	3 min	1
Denaturation	95	15 sec	40
Annealing	55	45 sec	
Extension	72	60 sec	

Calculation of the fold of gene expression

The fold expression versus the housekeeping gene and control was assessed using the Levak equation by following these procedures.

Ct (Control) – Ct (housekeeping control) = ΔCt (control) Ct (sample) – Ct (housekeeping sample) = ΔCt (sample) ΔCt (sample) – ΔCt (control) = ΔΔCt

Fold of gene expression = $(2^{-\Delta\Delta Ct})$

Statistical analysis

The data was analyzed using statistical analysis software, SPSS version 20, for the statistical analysis. The data are shown as mean±SD. Analysis of variance (ANOVA), *t* test, and correlation were used to perform the statistical analysis of the data. The threshold of significance was set at P≤0.05.

RESULTS

The total number of subjects that participated in the study was 60 (40 patients and 20 controls). Thirteen (32.5%) patients belonged to the 30–44 age group, seventeen (42.5%) to the 45–55 age group, and ten (25%) to the 56–70 age group. Table 3 shows that 5 patients (12.5%) were underweight (BMI<18.5), 12 patients (30%) had a normal weight (18.5–24.9), 14 patients (35%) were overweight (25–29.9), and 9 patients (22.5%) were obese (≥30).

Table 3. Distribution of Breast Cancer Women According to Age and Body Mass Index

Parameters		n	%
Age, y	30–45	13	32.5%
	45–55	17	42.5%
	56–70	10	25%
Body mass index, kg/m^2	Underweight (<18.5)	5	12.5%
	Normal weight (18.5–24.9)	12	30%
	Overweight (25–29.9)	14	35%
	Obese (≥30)	9	22.5%
Total	40 (100%)		

The results in Table 4 and Figure 1 show a statistically significant upregulation of both IL-2 (10.6±3.2pg/mL, 2.8±1.9pg/mL) and IL-8 (25.7±4.5pg/mL vs.8.3±1.0pg/mL) levels when comparing patients with breast cancer to the healthy group (P=0.003 and P=0.001, respectively).

Table 4. Mean Levels of Interleukins in Breast Cancer Patients Compared with the Control Group

Interleukins	Patients	Controls	P-value
IL-2 (pg/mL)	10.6±3.2	2.8±1.9	0.003
IL-8 (pg/mL)	25.7±4.5	8.3±1.0	0.001

A lower p53 titer (129.7±55.9) was seen in women with breast cancer compared to the control group (175.6±233.8) at a P-value of 0.02 (Table 5).

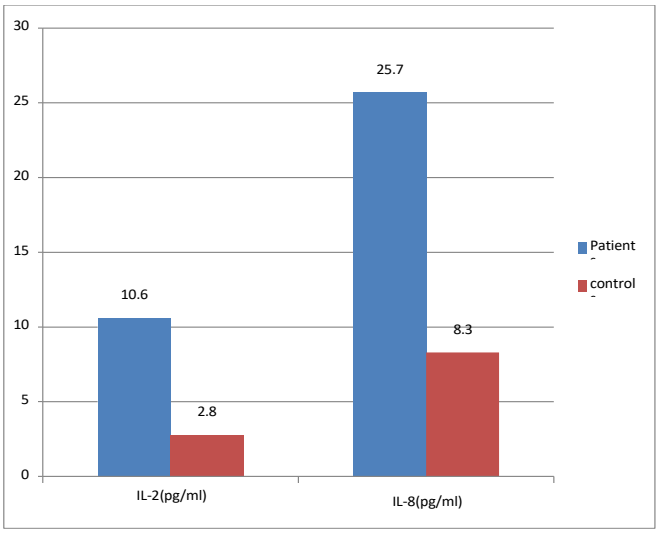

Figure 1. Mean Levels of Interleukins in Breast Cancer Patients Compared with the Control Group. IL, interleukin.

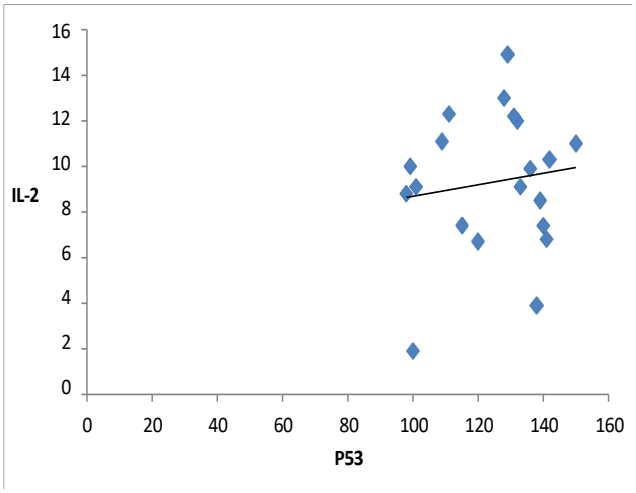

Figure 2. The Positive Correlation Between P53 and IL-2 in Breast Cancer Patients. IL, interleukin.

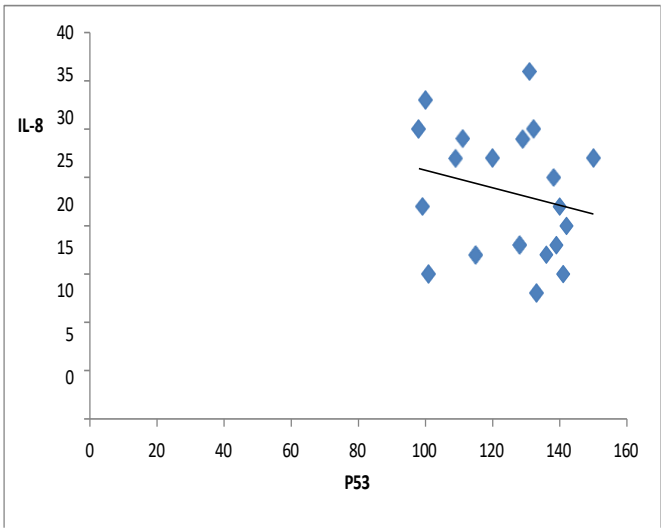

Figure 3. The Negative Correlation Between Serum P53 and IL-8 in Breast Cancer Patients. IL, interleukin.

A statistically significant positive correlation (r=0.01) between IL-2 and P53 titer is seen in Figure 2. However, a negative correlation (r=−0.02) can be seen between P53 titer and IL-8 (Figure 3). Nonetheless, a positive correlation exists between IL-2 and IL-8 (r=0.09) (Figure 4).

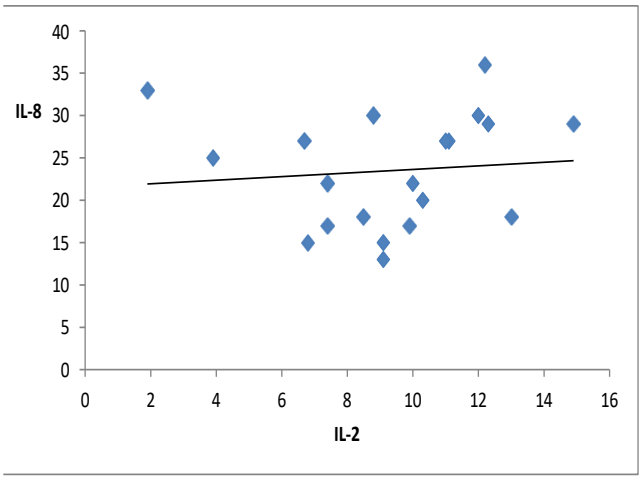

Figure 4. The Positive Correlation Between Serum IL-2 and IL-8 Concentrations in Breast Cancer Patients. IL, interleukin.

Table 5. Mean Level of P53 Titer in Breast Cancer Patients Compared to the Control Group

Parameter	Patients	controls	P-value
P53 titer	129.7±55.9	175.6±233.8	0.02

The results of the current study show variations in the results of P53 gene expression in 15 breast cancer patients compared to the control group, a difference which is significant at P=0.002 (Table 6 and Figure 5).

Table 6. P53 Gene Expression in Breast Cancer Patients Compared with the Control Group

Sample	Expression fold change ($2^{-\Delta\Delta Ct}$)
Control	1
Patient 1	0.241484082
Patient 2	0.10083022
Patient 3	0.291183397
Patient 4	1.443929196
Patient 5	0.200267469
Patient 6	0.334678110
Patient 7	0.10822034
Patient 8	0.450678008
Patient 9	0.200633209
Patient 10	0.350892001
Patient 11	1.233657790
Patient 12	0.153200304
Patient 13	1.199637009
Patient 14	0.400538668
Patient 15	1.60874425

DISCUSSION

The results of the current study are consistent with those of an Iraqi study by Al-Saady, who found that the BMI of breast cancer patients increased

significantly. [16] Four main reasons account for the correlation between obesity and breast cancer: (1) metabolism of sex hormones; (2) obese people have lower levels of circulating adiponectin; (3) a growth factor that promotes the proliferation of ERα-positive cells[17]; and (4) deregulated insulin signaling and chronic low-grade inflammation.[18] These findings indicate a higher incidence of breast cancer in patients aged 45 to 54 years, which is consistent with the findings reported by Khalil *et al.*[19] and Heer *et al.*[20] The highest incidence of illness was observed in women aged >48.[21] Since obesity increases the incidence of cancer with age, it is not surprising that a low incidence was observed in individuals younger than 40.[22] The increasing prevalence of breast cancer with age suggests that DNA methylation, a typical aspect of aging, may be one of the causes of increased breast cancer with age. The primary causes of elevated breast cancer in Asia include lifestyle factors, inadequate eating habits, and lack of screening.[23]

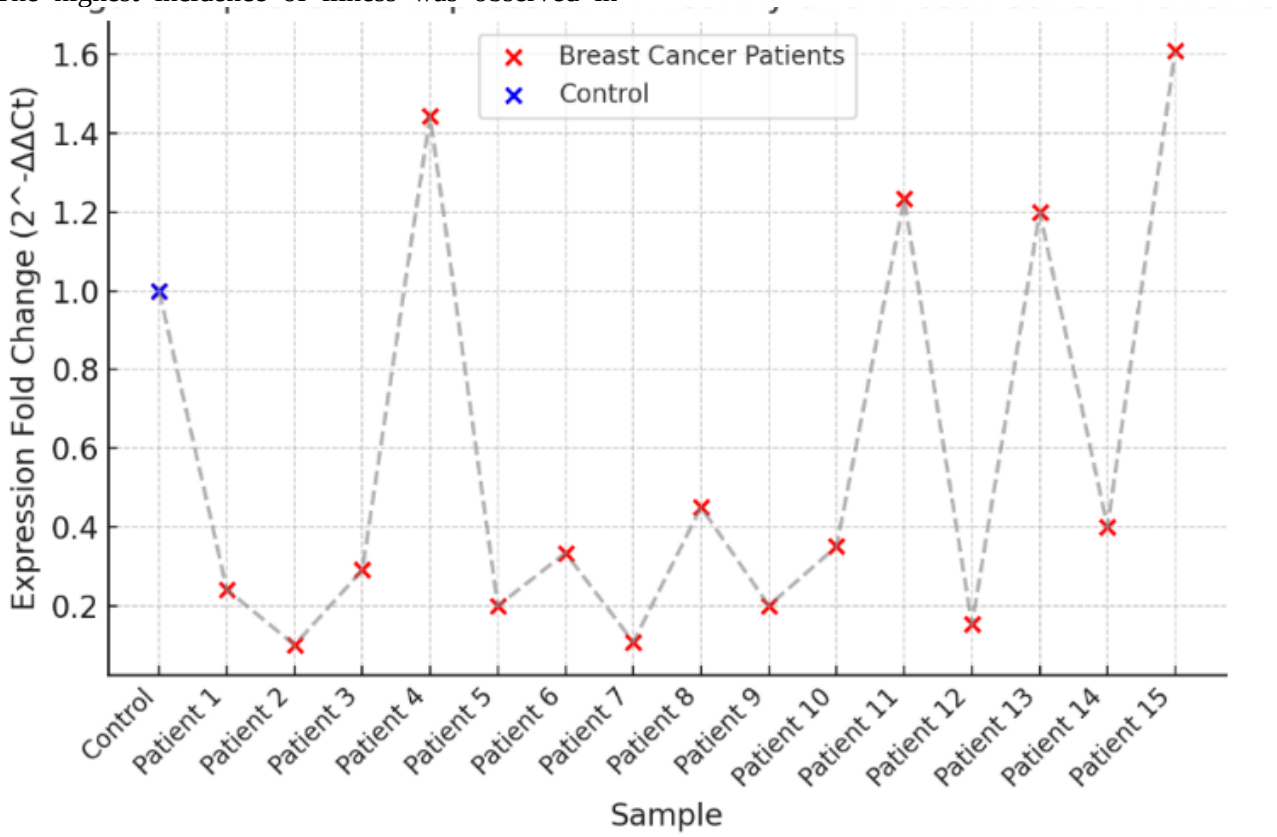

Figure 5. P53 gene expression in healthy and breast cancer participants

IL-2 showed an increase in breast cancer patients compared with the healthy group, which was in agreement with the results reported by Harjianti *et al.* and inconsistent with those reported by Al-Ghurabi *et al.*[24], which showed a decrease in serum levels of IL-2 in breast cancer patients compared with controls. Only T_H1 cells can produce IL-2, a lymphokine derived from T-cells. T_H1 cells secrete lymphokines that regulate cellular immunity, such as interferon (IFN-), tumor necrosis factor (TNF-), and IL-2, activating neutrophils, macrophages, and cytolytic cells.[25] Activation by IL-2, macrophages, neutrophils, and natural killer cells provides a nonspecific defense against tumors. Cell activation can have either cytostatic or cytolytic effects. These cells have the ability to eradicate all varieties of tumor cells because their immunity does not require antibodies or antigen specificity.[26]

A pleiotropic proinflammatory chemokine associated with inflammation, IL-8 (CXCL-8), influences angiogenesis and cancer growth, among other cellular processes. Additionally, this chemokine acts as an autocrine cytokine in tumors.[27] The current study's results showed a substantial increase in IL-8 levels in breast cancer patients compared to the control (P=0.001), a result that agrees with those of several other studies.[5,28] According to previous research, IL-8 promotes invasion and metastasis, and is overexpressed in a number of tumor cell types, including those that cause malignancies of the stomach and prostate.[29] Additionally, under some aberrant circumstances, tumor cells release IL-8, which promotes the protumorigenic processes of angiogenesis and cancer cell multiplication.[30]

In line with Kamel *et al.*, the p53 levels we observed were significantly different for the two

groups, with the control group having a higher mean than the patients,[31] which is at odds with research results reported by Al-Hassan *et al.*[32], who found a substantial rise in the mean serum level of p53-Ab in patients compared to controls. These genes regulate a variety of cellular processes and act as core modules of p53-repressed genes in breast cancer cells by simultaneously responding to genotoxic stress. The expression of p53 in breast cancer ranges from 9% to 69%.[33] The p53 mutation type may be determined by genetic or environmental factors, which may account for the increased expression of p53.[31]

The transfer of combinations of genes producing growth suppressors and immunomodulatory properties may serve as the foundation for novel approaches to enhance tumor regression in vivo. In a transgenic mouse breast model, Pützer *et al.*[34] examined the efficacy of combination therapy with Ad-vectors expressing p53, a tumor suppressor, and IL-2, an immune stimulator. Murine cells efficiently produced both genes, and Adp53wt-infected cells underwent apoptosis and showed significantly inhibited cell proliferation. When Adp53wt and AdIL-2 were combined, the dosage of the latter could be lowered without causing IL-2-related toxicity and without compromising its ability to completely eradicate tumors. The results found by Yaun *et al*.,[35] suggest that abnormal p53 expression may be important for modulating angiogenesis, VEGF, and IL-8 expression, which also explains why tumors with high aberrant p53 expression have a poor prognosis.[36] P53 regulates the expression of genes related to DNA repair, apoptosis (programmed cell death), and cell cycle regulation. This regulation is essential for preventing damaged DNA-containing cells from proliferating and possibly developing into cancer.[36] Also, p53 activity is often elevated in cells in which DNA damage is observed. In addition, it encourages DNA repair in that if the damage is too great, apoptosis is triggered to prevent the damaged cells from proliferating.[37] Finally, P53 is frequently mutated in various malignancies, including breast cancer. These mutations may result in a lack of tumor suppressor properties, which would allow cells to grow unchecked and develop tumors.[38]

Eleven samples exhibiting low p53 expression were analyzed, and the findings align with numerous studies indicating that diminished p53 levels are frequently correlated with poorer prognosis and altered treatment responses in breast cancer patients. Research is available on how the steady-state level of p53 mRNA is significantly reduced in many breast cancer cases compared to that in normal breast tissue. This decrease in p53 mRNA levels can be attributed to epigenetic modifications such as methylation of the HoxA5 promoter, which consequently impedes p53 expression.[39] International research has emphasized that mutant variants of p53, which may exhibit reduced expression levels, are frequently associated with increased cancer invasiveness and metastasis, further emphasizing the crucial role of p53 in ensuring normal cellular functions.[40]

Four samples exhibiting high levels of p53 expression were obtained from the patients, and the results obtained were consistent with numerous studies indicating p53 overexpression. In some breast cancers, p53 protein overexpression often occurs in response to cellular stress or DNA damage. This indicates an underlying mutation in the p53 gene, as mutant forms of the protein tend to be more stable and accumulate within the cells. This accumulation was detectable using immunohistochemical (IHC) techniques on the tissue samples. Utilizing p53 IHC as a diagnostic tool not only aids in identifying the mutational status of *TP53* but also serves as a prognostic marker. High p53 expression levels, as detected by IHC, are frequently associated with high-grade tumors and may correlate with poor outcomes in patients with breast cancer. Tumors exhibiting intense p53 staining are often high-grade and display a negative estrogen receptor status, underscoring the link between p53 overexpression and aggressive tumor characteristics.[41,42]

CONCLUSION

The results showed that IL-2 and IL-8 are important biomarkers for prognosis and diagnosis and have a significant effect on the development of breast cancer. In fact, these cytokines are increased in the serum from cancer patients, and because of their critical functions in the pathogenesis of cancer, they may prove to be attractive targets for cutting-edge treatments aimed at treating breast cancer. *TP53* is mutated in approximately half of all human malignancies, including breast cancer. As human cancers frequently have p53 deficiency, this protein is a great choice for cancer treatment.

ACKNOWLEGMENT

None.

ETHICAL CONSIDERATIONS

The Helsinki Declaration and later amendments were applied for all procedures conducted in the current study. Prior to the study, patients were informed about the nature and aims of the study and signed an informed consent form. The protocol was approved by the Ethical Committee, College of Health and Medical Techniques, Gilgamesh University, Baghdad, Iraq code 2906 (dated 20/12/2023).

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None.

DATA AVAILABILITY
Data related to this study are presented in the article.

REFERENCES

1. Smolarz B, Nowak AZ, Romanowicz H. Breast Cancer—Epidemiology, Classification, Pathogenesis and Treatment (Review of Literature). *Cancers (Basel)*. 2022;14(10):2569. doi:10.3390/cancers14102569.
2. AL-Wandawi TK, Nasir NA, Abdulhadi ZT, Al Salihi K. Clinical and Diagnostic Study of Breast Cancer in Women and its Relation with Periodontal Disease. *Archives of Breast Cancer*. 2025;12(1):85-98. doi:10.32768/abc.202512185-98.
3. Fasoulakis Z, Kolios G, Papamanolis V, Kontomanolis EN. Interleukins Associated with Breast Cancer. *Cureus*. Published online November 5, 2018. doi:10.7759/cureus.3549.
4. Todorović-Raković N, Milovanović J. Interleukin-8 in Breast Cancer Progression. *Journal of Interferon & Cytokine Research*. 2013;33(10):563-570. doi:10.1089/jir.2013.0023.
5. Al-Hasso IK. Assessment of Serum Soluble Toll-like Receptor-4 and Interleukin-8 as Biomarkers in Patients with Breast Cancer. *Al-Rafidain Journal of Medical Sciences (ISSN 2789-3219)*. 2024;6(1):167-171. doi:10.54133/ajms.v6i1.568.
6. Levine AJ. P53 and The Immune Response: 40 Years of Exploration—A Plan for the Future. *Int J Mol Sci*. 2020;21(2):541. doi:10.3390/ijms21020541.
7. Karima Al Salihi, Ihsan Abdullah, S. L. Ang. Histological implication of p53 gene expression in oral squamous cell carcinoma. *Journal of cellular cancer*. 2016;8(1):60-69.
8. Levine AJ. The many faces of p53: something for everyone. *J Mol Cell Biol*. 2019;11(7):524-530. doi:10.1093/jmcb/mjz026.
9. Hafner A, Bulyk ML, Jambhekar A, Lahav G. The multiple mechanisms that regulate p53 activity and cell fate. *Nat Rev Mol Cell Biol*. 2019;20(4):199-210. doi:10.1038/s41580-019-0110-x.
10. Timofeev O. Editorial: Mutant p53 in Cancer Progression and Personalized Therapeutic Treatments. *Front Oncol*. 2021;11. doi:10.3389/fonc.2021.740578.
11. Harris SL, Levine AJ. The p53 pathway: positive and negative feedback loops. *Oncogene*. 2005;24(17):2899-2908. doi:10.1038/sj.onc.1208615.
12. Marei HE, Althani A, Afifi N, et al. p53 signaling in cancer progression and therapy. *Cancer Cell Int*. 2021;21(1):703. doi:10.1186/s12935-021-02396-8.
13. Karima Akool Al-Salihi, S. L. Ang, A. Azlina, M.S. Farini, H. Jaffar. Immunohistochemical and molecular genetic analysis of p 53 in oral squamous cell carcinoma (scc) in Hospital University Science Malaysia: a preliminary study. *Braz J Oral Sci*. 2008;7(24).
14. Levine AJ. Spontaneous and inherited TP53 genetic alterations. *Oncogene*. 2021;40(41):5975-5983. doi:10.1038/s41388-021-01991-3.
15. Philomena George. P53 HOW CRUCIAL IS ITS ROLE IN CANCER? *International Journal of Current Pharmaceutical Research* . 2011;3(2).
16. Al-Saady RK. The Impact of Body Mass Index and Some Trace Elements in Iraqi Women with Breast Cancer. *J Fac Med Baghdad*. 2016;57(4):312-315. doi:10.32007/jfacmedbagdad.574397.
17. Mauro L, Naimo GD, Gelsomino L, et al. Uncoupling effects of estrogen receptor α on LKB1/AMPK interaction upon adiponectin exposure in breast cancer. *The FASEB Journal*. 2018;32(8):4343-4355. doi:10.1096/fj.201701315R.
18. Matthews S, Thompson H. The Obesity-Breast Cancer Conundrum: An Analysis of the Issues. *Int J Mol Sci*. 2016;17(6):989. doi:10.3390/ijms17060989.
19. Khalil S, Hatch L, Price CR, et al. Addressing Breast Cancer Screening Disparities Among Uninsured and Insured Patients: A Student-Run Free Clinic Initiative. *J Community Health*. 2020;45(3):501-505. doi:10.1007/s10900-019-00767-x.
20. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler-Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population-based study. *Lancet Glob Health*. 2020;8(8):e1027-e1037. doi:10.1016/S2214-109X(20)30215-1.
21. Johnson KC, Houseman EA, King JE, Christensen BC. Normal breast tissue DNA methylation differences at regulatory elements are associated with the cancer risk factor age. *Breast Cancer Research*. 2017;19(1):81. doi:10.1186/s13058-017-0873-y.
22. Wu C, Li M, Meng H, et al. Analysis of status and countermeasures of cancer incidence and mortality in China. *Sci China Life Sci*. 2019;62(5):640-647. doi:10.1007/s11427-018-9461-5.
23. Portakal O, Özkaya Öz, Erden inal M, Bozan B, Koşan M, Sayek I. Coenzyme Q10 concentrations and antioxidant status in tissues of breast cancer patients. *Clin Biochem*. 2000;33(4):279-284. doi:10.1016/S0009-9120(00)00067-9.
24. Al-Ghurabi BH. IL-2 and IL-4 Serum Levels in Breast Cancer. *J Fac Med Baghdad*. 2009;51(3):300-303. doi:10.32007/jfacmedbagdad.5131130.
25. Essa S, Siddique I, Saad M, Raghupathy R. Modulation of Production of Th1/Th2 Cytokines in Peripheral Blood Mononuclear Cells and Neutrophils by Hepatitis C Virus Infection in Chronically Infected Patients. *Pathogens*. 2021;10(11):1519. doi:10.3390/pathogens10111519.
26. Muraro E, Martorelli D, Turchet E, et al. A different immunologic profile characterizes patients with HER-2-overexpressing and HER-2-negative locally

advanced breast cancer: implications for immune-based therapies. *Breast Cancer Research*. 2011;13(6):R117. doi:10.1186/bcr3060.
27. WANG YC, WANG ZH, YEN JH, et al. The Contribution of Interleukin-8 Rs4073 Genotypes to Triple Negative Breast Cancer Risk in Taiwan. *Anticancer Res*. 2022;42(8):3799-3806. doi:10.21873/anticanres.15870.
28. Al-Hasso IK. Assessment of Serum Soluble Toll-like Receptor-4 and Interleukin-8 as Biomarkers in Patients with Breast Cancer. *Al-Rafidain Journal of Medical Sciences (ISSN 2789-3219)*. 2024;6(1):167-171. doi:10.54133/ajms.v6i1.568.
29. Mohsin SAM, Al-Thwani AN. Clinical importance of interleukin-8 concentration in Iraqi breast cancer patients. . *Iraqi J Biotechnol 2012;11(1):133-140*. 2012;11(1):133-140.
30. MATSUI T, OJIMA A, HIGASHIMOTO Y, TAIRA J, FUKAMI K, YAMAGISHI SI. Pigment epithelium-derived factor inhibits caveolin-induced interleukin-8 gene expression and proliferation of human prostate cancer cells. *Oncol Lett*. 2015;10(4):2644-2648. doi:10.3892/ol.2015.3568.
31. Ghazwan Sabah Kamel, Salih Mahdi Salman, Walaa Najim Abood. Evaluation of P53 and Some Blood Parameters In Women Diagnosed With Breast Cancer. *Diyala Journal of Medicine*. 2019;17(1).
32. Al-Hassan Ahmed AA. Detection of serum anti-p53 antibodies in breast cancer patients. *Al-Mustansiriyah Journal of Science* . Published online 2011:7-12.
33. Børresen-Dale AL. *TP53* and breast cancer. *Hum Mutat*. 2003;21(3):292-300. doi:10.1002/humu.10174.
34. Pützer BM, Bramson JL, Addison CL, et al. Combination Therapy with Interleukin-2 and Wild-Type p53 Expressed by Adenoviral Vectors Potentiates Tumor Regression in a Murine Model of Breast Cancer. *Hum Gene Ther*. 1998;9(5):707-718. doi:10.1089/hum.1998.9.5-707.
35. Yuan A, Yu CJ, Luh KT, Kuo SH, Lee YC, Yang PC. Aberrant *p53* Expression Correlates With Expression of Vascular Endothelial Growth Factor mRNA and Interleukin-8 mRNA and Neoangiogenesis in Non–Small-Cell Lung Cancer. *Journal of Clinical Oncology*. 2002;20(4):900-910. doi:10.1200/JCO.2002.20.4.900.
36. Feroz W, Sheikh AMA. Exploring the multiple roles of guardian of the genome: P53. *Egyptian Journal of Medical Human Genetics*. 2020;21(1):49. doi:10.1186/s43042-020-00089-x.
37. Schumacher B, Pothof J, Vijg J, Hoeijmakers JHJ. The central role of DNA damage in the ageing process. *Nature*. 2021;592(7856):695-703. doi:10.1038/s41586-021-03307-7.
38. Engeland K. Cell cycle regulation: p53-p21-RB signaling. *Cell Death Differ*. 2022;29(5):946-960. doi:10.1038/s41418-022-00988-z.
39. Gasco M, Shami S, Crook T. The p53 pathway in breast cancer. *Breast Cancer Research*. 2002;4(2):70. doi:10.1186/bcr426.
40. Marei HE, Althani A, Afifi N, et al. p53 signaling in cancer progression and therapy. *Cancer Cell Int*. 2021;21(1):703. doi:10.1186/s12935-021-02396-8.
41. D Kandioler-Eckersberger, C Ludwig, M Rudas, et al. TP53 mutation and p53 overexpression for prediction of response to neoadjuvant treatment in breast cancer patients. *Clin Cancer Res* 2000;6(1):50-56.
42. Mohan A, Jindal B, Thakral RK, Ansari V, Sharma VK. Role of p53 as a prognostic marker in breast carcinoma and its correlation with tumor size, tumor grade and lymph node metastasis. *Indian Journal of Pathology and Oncology*. 2020;7(3):378-383. doi:10.18231/j.ijpo.2020.076.

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