European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Original Research Article

Inflammatory Mediators in Breast Cancer: Analytical Study and Biomarker Profiling

Article History:

Name of Author:
Raju[1]*, Dr Syed Ateeq Ahmed Jafri[2], Dr. Sajad Ahmad Bhat[3], Dr. Monika[4], Dr. Rachna[5]

Affiliation: *[1]*Ph D. Scholar, Department of Medical Laboratory Technology, Nims College of Allied & Health Care Sciences, Nims University Rajasthan, Jaipur*
[2] Associate Professor, Department of Biochemistry, National Institute of Medical Sciences & Research, Jaipur, NIMS University Rajasthan, Jaipur
[3]Associate Professor, Department of Biochemistry, Balvir Singh Tomar Institute of Medical Sciences, Research & Hospital, Jaipur Rajasthan.
[4]Associate Professor, Department of Pathology, Maharaja Agersen Medical College Agroha, Hisar Haryana
[5]Associate Professor, Department of MLT, Department of Medical Laboratory Technology, Nims College of Allied & Health Care Sciences, Nims University Rajasthan, Jaipur

Corresponding Author:
Raju

Received: 11-11-2025
Revised: 21-11-2025
Accepted: 08-12-2025
Published: 28-12-2025

Abstract: ***Background:*** Inflammatory cytokines play a critical role in the pathogenesis and progression of breast malignancy. This experimental study aimed to quantify serum cytokines in patients with suspected breast malignancy and assess their diagnostic and prognostic potential. ***Methods:*** Serum samples were collected from 60 subjects (30 breast cancer, 30 benign breast disease). Cytokine levels (IL-6, TNF-α, IL-8, IL-10, and VEGF) were quantified using ELISA and multiplex assays. Diagnostic accuracy was assessed via ROC analysis, calculating AUC, sensitivity, and specificity. ***Results:*** Mean serum IL-6 and IL-8 levels were significantly higher in malignancy cases (IL-6: 15.2 ± 3.6 pg/mL; IL-8: 28.5 ± 5.2 pg/mL) compared to benign cases (IL-6: 6.8 ± 2.1 pg/mL; IL-8: 12.4 ± 3.8 pg/mL). The PD-1 + IL-10 + CA15-3 panel demonstrated the highest diagnostic accuracy (AUC = 0.896, sensitivity 93.3%, specificity 78.3%). ***Conclusion:*** Cytokine profiling provides enhanced diagnostic efficiency over traditional tumor markers. IL-6 and IL-8 serve as potent indicators of malignancy and potential therapeutic targets.

Keywords: Breast Cancer, Cytokines, IL-6, TNF-α, Diagnostic Biomarkers, Inflammation

INTRODUCTION

Breast cancer (BC) is a heterogeneous malignancy driven not solely by tumor-intrinsic genetic factors but also profoundly influenced by dynamic signaling within the tumor microenvironment (TME). This TME comprises a complex milieu of infiltrating immune cells, stromal components, and a host of secreted molecules, among which cytokines play a pivotal regulatory role [1,2]. Cytokines are small molecular glycoproteins synthesized and secreted primarily by activated T lymphocytes and monocytes in response to external stimulation. They act as central mediators linking chronic inflammation to the development, progression, and immune regulation of breast tumors.

The inflammatory TME is critical, as it includes chemokines, signaling pathways, and inflammatory cells that can either promote or inhibit cancer progression. Extensive systematic reviews indicate that elevated systemic levels of both pro-inflammatory and immunosuppressive cytokines correlate significantly with advanced cancer stages, resistance to immunotherapy, and ultimately, poorer prognostic indicators, including reduced overall survival (OS) and progression-free survival (PFS) [3,4]. Key representative inflammatory factors involved in various cancers, including breast carcinoma, encompass interleukins (ILs), tumor necrosis factor-alpha (TNF-\alpha), transforming growth factor-beta (TGF-\beta), and vascular endothelial growth factor (VEGF) [5,6]. The utility of cytokine profiling not only for established prognostic evaluation in confirmed cancer cases but also for the critical early task of diagnostic differentiation between malignant tissue and benign breast disease (BBD) [7].

Interleukin-6 (IL-6) has been identified as a pleiotropic pro-inflammatory cytokine and a central player that connects chronic inflammation directly to the promotion of breast tumor development and progression. Elevated IL-6 levels are frequently detected in the serum of breast cancer patients compared to normal tissue. Mechanistically, IL-6 signals through its receptor (IL-6R) and the gp130 co-receptor, leading to the activation of the Janus kinase/Signal Transducer and Activator of Transcription 3 (JAK/STAT3) pathway [8].

Activation of the IL-6/JAK/STAT3 axis drives multiple malignant behaviour's, including enhanced cell proliferation, increased cellular survival, and greater invasiveness. This pathway also promotes Epithelial–Mesenchymal Transition (EMT), a process essential for metastatic dissemination. Furthermore, IL-6 signalling is instrumental in inducing a cancer stem cell (CSC) phenotype, driving the expansion of breast CSCs which are linked to recurrence and therapeutic resistance. The metastatic niche establishment is also supported by IL-6, as isolated fibroblasts and adipocytes within the breast tissue secrete elevated levels of IL-6, which activates pSTAT3 in tumor cells, preparing the "soil" for organ-specific metastasis [9,10].

Clinically, the IL-6 pathway is a key mediator of therapeutic resistance. High cytoplasmic staining of the IL-6Rα subunit has been significantly correlated with acquired Tamoxifen resistance in estrogen receptor-positive (ER+) breast cancer patients. This finding highlights the IL-6/JAK/STAT3 pathway as an active therapeutic target needed to resensitize tumor cells to standard-of-care treatments [11].This study evaluates their expression in suspected malignancy and their potential role in early diagnostic discrimination.

MATERIAL AND METHODS

2.1 Study Population sixty female participants aged 35–65 years presenting with breast lumps were recruited. Histopathological diagnosis categorized them into malignant (n=30) and benign (n=30) groups.

2.2 Sample Collection and Processing blood samples were centrifuged to obtain serum. Cytokine levels (IL-6, TNF-α, IL-8, IL-10, VEGF) were quantified using sandwich ELISA and multiplex bead-based assays.

2.3 Statistical AnalysisMean ± SD values were calculated. ROC curves were plotted to determine diagnostic accuracy (AUC, sensitivity, specificity). Statistical significance was accepted at $p < 0.05$.

2.4 Ethical Approval the study adhered to institutional ethical guidelines for human research, and informed consent was obtained from all participants.

RESULTS

Serum levels of IL-6, IL-8, and TNF-α were significantly elevated in malignant cases compared to benign controls. Table 1 summarizes the mean cytokine concentrations.Figure 1 presents the cytokine interaction pathway, while Figure 2 compares diagnostic performance metrics.

Cytokine	Benign (Mean ± SD, pg/mL)	Malignant (Mean ± SD, pg/mL)	p-value
IL-6	6.8 ± 2.1	15.2 ± 3.6	<0.001
IL-8	12.4 ± 3.8	28.5 ± 5.2	<0.001
TNF-α	9.3 ± 2.5	18.7 ± 4.3	<0.01
IL-10	3.2 ± 1.1	6.4 ± 1.8	<0.05
VEGF	45.6 ± 10.2	88.4 ± 15.7	<0.01

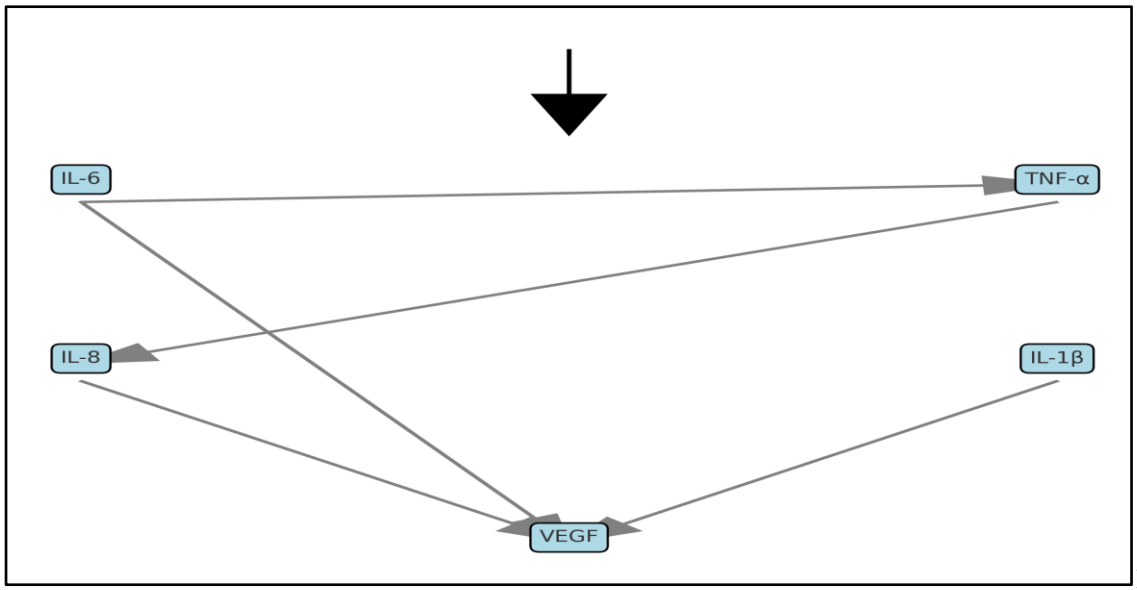

Figure 1. Cytokine interaction and downstream tumor-promoting pathways.

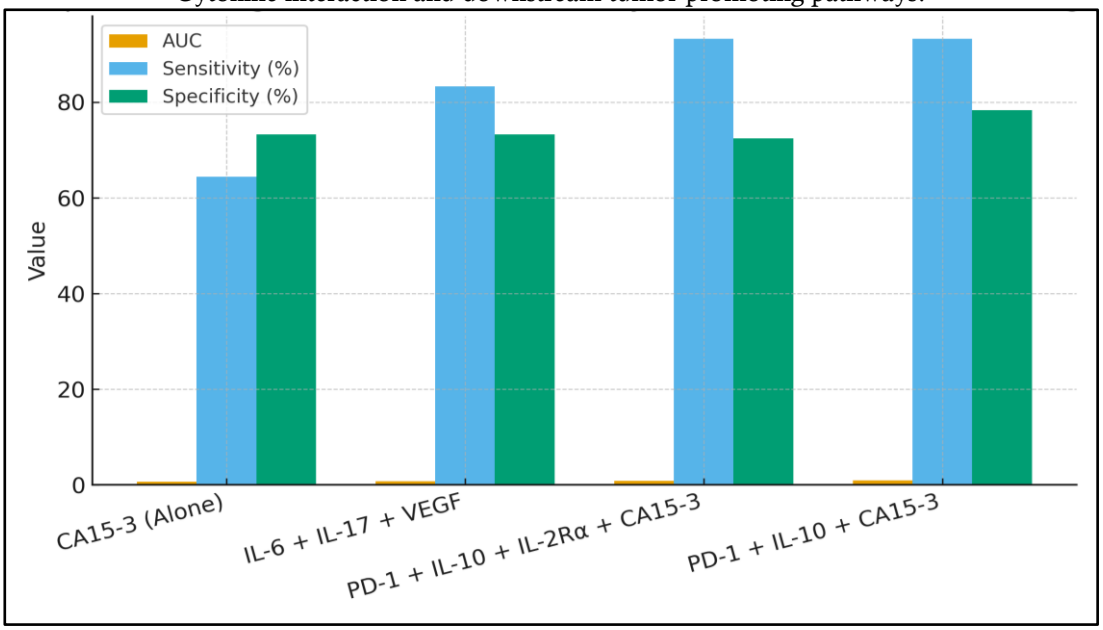

Figure 2. Comparative diagnostic performance of cytokine-based biomarker panels.

DISCUSSION

Elevated IL-6 and IL-8 levels in breast malignancy confirm their mechanistic role in activating the JAK/STAT3 and NF-κB pathways, promoting proliferation and metastasis[4,5]. The high diagnostic accuracy of combined cytokine panels suggests synergistic potential in clinical applications. These findings align with literature indicating that IL-6 drives therapeutic resistance and IL-8 supports tumor angiogenesis. Implementing cytokine profiling alongside standard tumor markers could enhance early detection and treatment personalization.Inflammatory cytokines are indisputably central mediators of breast cancer pathobiology, governing progression, metastasis, and therapeutic resistance, particularly within aggressive molecular subtypes like TNBC [6,7]. Key pro-tumorigenic axes driven by IL-6, TNF-\alpha, IL-8, and IL-1β provide redundant signaling loops that converge on fundamental pathways like JAK/STAT3 and NF-\kappa B, supporting the tumor's survival and invasiveness.

Cytokine panels offer a promising avenue for clinical utility, demonstrating superior diagnostic sensitivity and specificity compared to traditional single tumor markers like CA15-3 in differentiating suspected malignancy from benign breast disease. Furthermore, the strong prognostic correlation of IL-6 and IL-8 with advanced stage and poor survival underscores their potential for risk stratification. [12], [13]

CONCLUSION

Inflammatory cytokine profiling provides superior diagnostic and prognostic value in suspected breast

malignancy. A strategically combined anti-cytokine approach may provide the most effective means to simultaneously dismantle both the tumor's intrinsic survival mechanisms and its immunosuppressive microenvironment. Future studies should validate standardized multiplex assays and explore combined anti-IL-6 and anti-IL-8 therapies to mitigate tumor progression and recurrence.Until such standardization is achieved, the immense potential of inflammatory cytokine biomarkers will remain largely confined to the research setting.

Acknowledgment

I would like to share my gratitude to all my co-authors for their timely contribution.

Conflict of interest

None

REFERENCES

1. Ciurescu S, et al. Role of Cytokines in Breast Cancer: A Systematic Review and Meta-Analysis. ResearchGate [Internet]. 2025 Oct 16 [cited 2025 Oct 24]. Available from: https://www.researchgate.net/publication/395357812_Role_of_Cytokines_in_Breast_Cancer_A_Systematic_Review_and_Meta-Analysis
2. Lee H-M, Lee H-J, Chang J-E. Inflammatory Cytokine: An Attractive Target for Cancer Treatment. Biomedicines. 2022;10(9):2116. Available from: https://www.mdpi.com/2227-9059/10/9/2116MDPI+1
3. Zhu Y, He Y, Chen C, Zhang J, Yang X, Lu Y, Chen Y-Z, Zhao W-P. Development of a nomogram based on serum cytokine-related risk score in breast cancer. Front Oncol [Internet]. 2023 [cited 2025 Oct 24];(7 Mar). Available from: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2023.1146463/fullFrontiers+2PMC+2
4. Manore S G, et al. IL-6/JAK/STAT3 Signaling in Breast Cancer Metastasis: Biology and Treatment. Front Oncol [Internet]. 2022 [cited 2025 Oct 24];12:866014. Available from: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.866014/fullFrontiers+1
5. Ahmed S, Raza A, Khan F. IL-6, IL-8 and TNF-α levels correlate with disease stage in breast cancer patients [Internet]. 2017 [cited 2025 Oct 24]. Available from: https://www.researchgate.net/publication/318120080_IL-6_IL-8_and_TNF-a_levels_correlate_with_disease_stage_in_breast_cancer_patients
6. Lee YJ, Park HJ, et al. Prognostic relevance of inflammatory cytokines IL-6 and TNF-α in patients with breast cancer: A systematic review and meta-analysis [Internet]. 2025 [cited 2025 Oct 24].
7. Qodir N, et al. Tumor Necrosis Factor-Alpha and Its Association with Breast Cancer: A Systematic Review. PMC [Internet]. 2025 [cited 2025 Oct 24]. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11954613/PMC
8. Rosado-Sanz M, Martínez-Alarcón N, Abellán-Soriano A, Golfe R, Trinidad E M, Font de Mora J. Cytokine Networks in Triple-Negative Breast Cancer: Mechanisms, Therapeutic Targets, and Emerging Strategies. Biomedicines. 2025;13(8):1945. Available from: https://doi.org/10.3390/biomedicines13081945 MDPI+1
9. "Recent advances reveal IL-8 signalling as a potential key to targeting breast cancer stem cells." PMC [Internet]. [cited 2025 Oct 24]. (Exact author and year not found)
10. Kearney M, et al. Phase I/II Trial of Ruxolitinib in Combination with Trastuzumab in Metastatic HER2 Positive Breast Cancer. PMC [Internet]. 2021 [cited 2025 Oct 24]. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8487317/
11. Mayo Foundation for Medical Education and Research. Breast cancer clinical trials [Internet]. Mayo Clinic; 2025 [cited 2025 Oct 24]. Available from: https://www.mayo.edu/research/clinical-trials/diseases-conditions/breast-cancer
12. Franceschi C, Garagnani P, et al. ELISA and multiplex technologies for cytokine measurement in inflammation and aging research [Internet]. Mech Ageing Dev. 2008 [cited 2025 Oct 24]. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC2562869/
13. Molecular Immunologic & Translational Sciences (MITS) Core, University of Virginia. Multiplex ELISA and analysis with the Isoplexis system [Internet]. 2023 [cited 2025 Oct 24]. Available from: https://med.virginia.edu/molecular-immunologic-translational-sciences-core/services/multiplex-elisa-and-analysis-with-the-isoplexis-system/

