Electronic Journal of University of Aden for Basic and Applied Sciences

EJUA-BA Vol. 7 No. 2 (2026)

https://doi.org/10.47372/ejua-ba.2026.2.540

ISSN: 2708-0684

RESEARCH ARTICLE

SERUM FERRITIN, LDH, AND CRP AS POTENTIAL PROGNOSTIC BIOMARKERS IN BREAST CANCER: ASSOCIATION WITH TUMOR GRADE, STAGE, AND RECEPTOR STATUS

Naji Ahmed Naji Salem[1,*], and Gamal Abdul-Hamid[1]

[1] *Dept. of Paraclinic, Faculty of Medicine and Health Sciences, University of Aden, Yemen*

***Corresponding author: Naji Ahmed Naji Salem; E-mail: drnajiahmed1234@gmail.com**

Received: 06 April 2026 / Accepted: 17 May 2026 / Published online: 30 June 2026

Abstract

Inflammatory biomarkers such as serum ferritin, lactate dehydrogenase (LDH), and C-reactive protein (CRP) have been implicated in cancer progression and prognosis. This study aimed to evaluate their association with clinicopathological characteristics in breast cancer patients from Yemen. A cross-sectional analysis of 150 breast cancer patients (60 newly diagnosed, 90 managed) was conducted. Serum levels of ferritin, LDH, and CRP were measured and correlated with tumor size, grade, lymph node status, hormone receptor status, and human epidermal growth factor receptor 2 (HER2) expression. Serum ferritin, LDH, and CRP levels were significantly elevated in patients with higher tumor grade (Grade III), advanced tumor stage (T3/T4), lymph node involvement (N2/N3), and metastatic disease ($p<0.05$). Ferritin levels were higher in HER2-positive and progesterone receptor-positive tumors. CRP was elevated in estrogen receptor-negative and progesterone receptor-negative subgroups in managed cases. All three markers showed a stepwise increase with advancing tumor burden. Managed patients had significantly lower levels of all markers compared to newly diagnosed patients, indicating treatment response. Serum ferritin, LDH, and CRP are significantly associated with aggressive tumor features in breast cancer. These inexpensive and readily available biomarkers may serve as useful prognostic tools, particularly in resource-limited settings like Yemen, to stratify risk and monitor treatment response.

Keywords: Breast cancer; Ferritin; Lactate dehydrogenase; C-reactive protein; Prognostic biomarkers; Yemen; Tumor stage; Hormone receptors.

Introduction

Breast cancer remains a leading cause of cancer-related mortality among women globally, with prognosis heavily influenced by tumor biology and stage at diagnosis [1]. In low-resource settings such as Yemen, access to advanced molecular profiling and imaging is limited, necessitating the identification of affordable and accessible biomarkers for risk stratification and treatment monitoring [2-4]. Systemic inflammation plays a well-established role in cancer progression, metastasis, and treatment resistance [5]. Consequently, inflammatory biomarkers have emerged as potential prognostic indicators in various malignancies, including breast cancer [6].

Serum ferritin, traditionally a marker of iron stores, is also an acute-phase reactant elevated in chronic inflammation and malignancy [7]. Elevated ferritin has been associated with poor prognosis in breast cancer, potentially reflecting tumor aggressiveness and inflammatory burden [8]. Lactate dehydrogenase (LDH), a glycolytic enzyme released during tissue damage, is often elevated in aggressive tumors and is linked to hypoxia, angiogenesis, and metastasis [9]. Similarly, C-reactive protein (CRP), a classic acute-phase protein, correlates with systemic inflammation and has been implicated in cancer-related outcomes [10].

Despite growing evidence of their prognostic value, data on the association of these biomarkers with detailed clinicopathological features, particularly in underrepresented populations such as Yemeni patients, remain scarce. This study aimed to evaluate serum ferritin, LDH, and CRP levels in relation to tumor grade, stage, lymph node involvement, hormone receptor status, and HER2 expression in a cohort of breast cancer patients from Yemen. We also compared biomarker levels between newly diagnosed and managed patients to assess treatment-related changes.

Materials and Methods

Study Design and Population

This cross-sectional study included 150 female breast cancer patients treated at the National Oncology Center, Aden, Yemen, between January and December 2022. Patients were categorized into newly diagnosed (n=60, before any treatment) and managed (n=90, receiving or having completed treatment) groups. Ethical approval was obtained, and informed consent was secured from all participants.

Data Collection

Demographic and clinicopathological data were extracted from medical records. Tumor characteristics included size (T1–T4), grade (I–III), lymph node status (N0–N3), estrogen receptor (ER), progesterone receptor (PR), and HER2 status. Metastasis status was recorded as present or absent.

Laboratory Measurements

Venous blood samples were collected after an overnight fast. Serum ferritin was measured by chemiluminescent immunoassay, LDH by enzymatic method, and CRP by immunoturbidimetric assay, following standard protocols.

Statistical Analysis

Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± SD and compared using Student's t-test or ANOVA. Categorical variables were compared using chi-square tests. Pearson correlation was used to assess relationships between biomarkers and tumor characteristics. A p-value <0.05 was considered statistically significant.

Results

Baseline Characteristics

The mean age of participants was 48.9 ± 11.2 years. Most tumors were invasive ductal carcinoma (85.3%), Grade II (48.7%), and T2 stage (52.7%). Lymph node involvement was present in 64.7% of cases, and metastasis in 44.7%. ER and PR positivity were observed in 67.3% and 60.0% of patients, respectively; 35.3% were HER2-positive.

Association of Ferritin, LDH, and CRP with Tumor Characteristics

Table 1: Serum ferritin levels according to tumor characteristics

Characteristic	Newly Diagnosed (ng/mL)	Managed Cases (ng/mL)	p-value (Between Groups)
Grade I	171.7 ± 83.9	144.1 ± 87.2	0.479
Grade II	193.9 ± 118.1	146.1 ± 114.1	0.085
Grade III	292.3 ± 262.1	168.8 ± 137.7	0.031
T1	172.5 ± 83.3	95.1 ± 42.4	0.002
T2	183.0 ± 105.8	157.7 ± 115.9	0.343
T3	300.8 ± 246.6	167.0 ± 118.9	0.096
T4	709.0 ± 439.8	253.9 ± 185.7	0.126
Metastasis Yes	288.1 ± 243.3	195.0 ± 152.1	0.060
Metastasis No	170.2 ± 85.0	121.6 ± 75.1	0.008

Comment: Ferritin levels increased with tumor grade and size and were higher in metastatic disease. Managed patients had lower ferritin across most subgroups.

Table 2: Serum LDH levels according to tumor characteristics

Characteristic	Newly Diagnosed (U/L)	Managed Cases (U/L)	p-value (Between Groups)
Grade I	183.3 ± 64.9	174.2 ± 38.9	0.682
Grade II	291.8 ± 95.8	235.8 ± 70.2	0.006
Grade III	303.5 ± 109.6	247.7 ± 74.5	0.032
T1	194.3 ± 79.1	193.9 ± 43.3	0.984
T2	271.4 ± 82.9	228.6 ± 67.8	0.016
T3	346.2 ± 106.8	279.7 ± 78.2	0.056
Metastasis Yes	323.9 ± 99.4	262.2 ± 87.8	0.009
Metastasis No	228.5 ± 90.3	209.2 ± 46.6	0.203

Comment: LDH showed a clear gradient with increasing grade and stage. Managed patients had significantly lower LDH in higher-grade and metastatic subgroups.

Table 3: Serum CRP levels according to tumor characteristics

Characteristic	Newly Diagnosed (mg/L)	Managed Cases (mg/L)	p-value (Between Groups)
Grade I	6.0 ± 7.78	5.5 ± 3.89	0.863
Grade II	12.3 ± 11.12	6.3 ± 6.59	0.005
Grade III	20.7 ± 20.30	13.4 ± 14.07	0.131
T1	5.8 ± 6.53	5.4 ± 7.28	0.859
T2	11.5 ± 10.59	6.8 ± 6.10	0.014
T3	24.1 ± 21.16	14.7 ± 13.89	0.153
Metastasis Yes	22.4 ± 19.02	11.9 ± 13.75	0.011
Metastasis No	6.7 ± 4.95	6.1 ± 5.04	0.637

Comment: CRP levels rose with tumor grade and stage and were significantly higher in metastatic disease. Managed patients showed lower CRP in intermediate-grade and metastatic subgroups.

Biomarkers and Receptor Status

Ferritin was higher in PR-positive tumors in newly diagnosed cases (p=0.037). CRP was higher in PR-positive newly diagnosed cases (p=0.045) but higher in PR-negative managed cases (p=0.004). In managed cases, ER-negative and PR-negative tumors had higher CRP (p<0.01). HER2-positive tumors had higher ferritin and LDH in newly diagnosed patients (p<0.05).

Correlation Between Biomarkers and Tumor Burden

All three markers showed positive correlations with tumor size, nodal status, and presence of metastasis (p<0.05). Ferritin correlated strongly with LDH (r=0.553, p<0.001) and CRP (r=0.242, p=0.036) in newly diagnosed patients.

Comparison Between Newly Diagnosed and Managed Patients

Managed patients had significantly lower mean ferritin (152.6 vs. 227.2 ng/mL, p=0.003), LDH (231.6 vs. 274.6 U/L, p=0.039), and CRP (8.6 vs. 14.3 mg/L, p=0.049) compared to newly diagnosed patients, suggesting treatment-related reduction.

Discussion

This study demonstrates that serum ferritin, LDH, and CRP are significantly associated with aggressive clinicopathological features in breast cancer, including higher grade, advanced stage, lymph node involvement, and metastatic disease. Our findings align with and extend previous research on inflammatory biomarkers in oncology, particularly within an underserved Yemeni population.

Ferritin as a Marker of Tumor Aggressiveness

Elevated serum ferritin has been previously linked to poor prognosis in breast cancer. A meta-analysis by Wang et al. (2019) concluded that high ferritin levels correlate with larger tumor size, nodal metastasis, and reduced survival [8]. Our results are consistent, showing stepwise increases in ferritin with tumor grade and stage. The association between ferritin and HER2-positive disease is notable, as HER2-positive tumors are often more aggressive [11]. The mechanism may involve iron-mediated oxidative stress promoting tumor proliferation [12].

LDH: A Reflector of Metabolic Activity and Hypoxia

LDH is a key enzyme in anaerobic glycolysis, often upregulated in hypoxic tumor microenvironments. Elevated LDH has been consistently associated with advanced disease and poor outcomes in breast cancer [9]. Our findings of higher LDH in Grade III and metastatic tumors mirror studies from India and China, where LDH served as a reliable marker of disease burden [13,14]. The reduction in LDH in managed patients suggests treatment may normalize tumor metabolism, a phenomenon observed in other cohorts [15].

CRP and Systemic Inflammation

CRP, a nonspecific inflammatory marker, has been validated as a prognostic factor in multiple cancers. Elevated CRP correlates with advanced stage, hormone receptor negativity, and shorter survival in breast cancer [10,16]. Interestingly, we observed higher CRP in hormone receptor-negative tumors among managed patients, which may reflect a more inflamed, treatment-resistant phenotype [17]. This aligns with studies showing that basal-like and triple-negative breast cancers are associated with higher inflammatory markers [18].

Comparison with Regional and Global Studies

Studies from the Middle East have reported similar trends. In Saudi Arabia, elevated ferritin and LDH were linked to advanced breast cancer [19]. In Egypt, CRP and LDH predicted chemotherapy response [20]. Our Yemeni cohort shows comparable patterns, reinforcing the universality of these biomarkers despite geographic and ethnic differences.

Clinical Implications in Low-Resource Settings

In Yemen, where access to advanced diagnostics is limited, ferritin, LDH, and CRP offer inexpensive, routinely available tools for risk stratification and treatment monitoring. Integrating these biomarkers into clinical algorithms could help identify high-risk patients needing intensive therapy and monitor response in real-time.

Conclusion

Serum ferritin, LDH, and CRP are strongly associated with adverse clinicopathological features in breast cancer and decrease following treatment. These biomarkers may serve as valuable prognostic tools, particularly in resource-limited settings like Yemen, to guide risk-adapted therapy and monitor treatment response. Further validation in larger, prospective cohorts is recommended.

References

[1] F. Bray, J. Ferlay, I. Soerjomataram, et al., "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries," CA Cancer J. Clin., vol. 68, no. 6, pp. 394–424, 2018.

[2] G. A. Hamid, "Breast cancer care in Yemen," Eur. J. Pharm. Med. Res., vol. 9, no. 3, pp. 24–29, 2022.

[3] W. Al-kahiry, H. H. Omer, N. M. Saeed, and G. A. Hamid, "Late presentation of breast cancer in Aden, Yemen," Gulf J. Oncol., vol. 1, no. 9, pp. 7–11, 2011.

[4] A. Bawazir, H. Basaleem, A. Badheeb, and G. Abdul Hamid, "General oncology care in the Republic of Yemen," in Cancer in the Arab World, H. Al-Shamsi, I. Abu-Gheida, F. Iqbal, and A. Al-Awadhi, Eds. Springer, 2022, pp. 321–338. [Online]. Available: https://doi.org/10.1007/978-981-16-7945-2_20

[5] C. I. Diakos, K. A. Charles, D. C. McMillan, et al., "Cancer-related inflammation and treatment effectiveness," Lancet Oncol., vol. 15, no. 11, pp. e493–e503, 2014.

[6] J. M. Almeida, M. Fonseca, and A. I. Santos, "The role of inflammatory biomarkers in breast cancer prognosis: A systematic review," Clin. Chim. Acta, vol. 461, pp. 1–9, 2016.

[7] L. G. Coffman, D. Parsonage, R. D'Agostino Jr, et al., "Regulatory effects of ferritin on angiogenesis," Proc. Natl. Acad. Sci. USA, vol. 106, no. 2, pp. 570–575, 2009.

[8] W. Wang, H. Wang, X. Zhang, et al., "Serum ferritin as a prognostic marker in breast cancer: a meta-analysis," Breast Cancer Res. Treat., vol. 176, no. 3, pp. 491–499, 2019.

[9] J. E. Brown, R. J. Cook, A. Lipton, et al., "Lactate dehydrogenase as a prognostic marker in metastatic breast cancer: a systematic review," Breast, vol. 52, pp. 100–108, 2020.

[10] K. H. Allin, S. E. Bojesen, and B. G. Nordestgaard, "Elevated baseline C-reactive protein levels and poor prognosis in cancer patients: a systematic review and meta-analysis," PLoS One, vol. 6, no. 12, p. e27162, 2011.

[11] D. J. Slamon, G. M. Clark, S. G. Wong, et al., "Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene," Science, vol. 235, no. 4785, pp. 177–182, 1987.

[12] S. V. Torti and F. M. Torti, "Iron and cancer: more ore to be mined," Nat. Rev. Cancer, vol. 13, no. 5, pp. 342–355, 2013.

[13] S. Kumar, A. K. Singh, and A. Verma, "Lactate dehydrogenase as a prognostic marker in breast cancer: an Indian perspective," Indian J. Cancer, vol. 55, no. 2, pp. 178–182, 2018.

[14] J. Li, X. Zhang, and Y. Wang, "Correlation between LDH and tumor characteristics in breast cancer patients," Cancer Biomark., vol. 20, no. 2, pp. 145–151, 2017.

[15] M. El-Fatatry, A. A. Hassan, and S. H. El-Shorbagy, "Inflammatory markers and response to chemotherapy in Egyptian breast cancer patients," J. Egypt. Natl. Canc. Inst., vol. 34, no. 1, p. 15, 2022.

[16] L. Guo, Y. Wang, and X. Zhang, "The relationship between inflammatory markers and tumor characteristics in breast cancer," Oncol. Lett., vol. 10, no. 4, pp. 2329–2334, 2015.

[17] A. Mohammadi, M. Ghasemi, and S. Khosravi, "Association of hematological parameters with inflammatory markers in breast cancer patients in Iran," Iran. J. Cancer Prev., vol. 13, no. 1, p. e100968, 2020.

[18] C. Desmedt, B. Haibe-Kains, P. Wirapati, et al., "Biological processes associated with breast cancer clinical outcome depend on the molecular subtypes," Clin. Cancer Res., vol. 14, no. 16, pp. 5158–5165, 2008.

[19] F. M. Alsharif, A. A. Aljohani, and A. S. Alzahrani, "Impact of chemotherapy on inflammatory markers in Saudi breast cancer patients," Saudi Med. J., vol. 42, no. 6, pp. 634–640, 2021.

[20] A. Raza, H. J. Malik, and S. Saeed, "Patterns of inflammatory markers in breast cancer patients before and after chemotherapy in Pakistan," Asian Pac. J. Cancer Prev., vol. 22, no. 3, pp. 789–795, 2021.

مقالة بحثية

الفريتين في المصل، ونازعة هيدروجين الالكتات LDH، والبروتين التفاعلي CRP C كعوامل تنبؤية محتملة في سرطان الثدي: الارتباط مع درجة الورم والمرحلة وحالة المستقبلات

ناجي احمد ناجي سالم[1،*]، و جمال عبدالحميد[2]

[1] قسم الباركلينك، كلية الطب والعلوم الصحية، جامعة عدن، اليمن

* الباحث الممثل: ناجي احمد ناجي سالم؛ البريد الالكتروني: drnajiahmed1234@gmail.com

استلم في: 06 ابريل 2026 / قبل في: 17 مايو 2026 / نشر في 30 يونيو 2026

المُلخّص

لقد تضمنت المؤشرات الحيوية الالتهابية مثل الفريتين في المصل، ونازعة هيدروجين الالكتات LDH، والبروتين التفاعلي CRP C في تطور السرطان وتوقعاته. هدفت هذه الدراسة إلى تقييم ارتباطها بالخصائص السريرية المرضية لدى مرضى سرطان الثدي في اليمن. أجري تحليل مقطعي لـ 150 مريضة بسرطان الثدي (60 تم تشخيصها حديثًا، و 90 تحت العلاج). تم قياس مستويات الفريتين و LDH و CRP في المصل وربطها بحجم الورم ودرجته وحالة العقد الليمفاوية وحالة مستقبلات الهرمون وتعبير مستقبل عامل النمو البشري 2 (HER2). كانت مستويات الفريتين و LDH و CRP في المصل مرتفعة بشكل ملحوظ لدى المرضى الذين يعانون من درجة ورم أعلى الدرجة الثالثة، ومرحلة ورم متقدمة (T4/T3)، وتورم العقد الليمفاوية (N3/N2)، ومرض نقيلي ($p>05.0$). كانت مستويات الفريتين أعلى في الأورام الإيجابية لـ HER2 والإيجابية لمستقبلات البروجسترون. ارتفع CRP في المجموعات الفرعية السلبية لمستقبلات الأستروجين والسلبية لمستقبلات البروجسترون في الحالة التي كانت تحت العلاج. أظهرت جميع المؤشرات الثالثة زيادة تدريجية مع تقدم عبء الورم. كان لدى المرضى الذين كانوا تحت العلاج مستويات أقل بكثير من جميع المؤشرات مقارنة بالمرضى الذين تم تشخيصهم حديثًا، مما يشير الى الاستجابة للعلاج. يرتبط الفريتين في المصل و LDH و CRP بشكل كبير بسمات الورم العدوانية في سرطان الثدي. قد تكون هذه المؤشرات الحيوية غير المكلفة والمتاحة بسهولة أدوات تنبؤ مفيدة، خاصة في الأماكن محدودة الموارد مثل اليمن، لتحديد المخاطر ومراقبة الاستجابة للعلاج.

الكلمات المفتاحية: سرطان الثدي؛ فريتين؛ نازعة هيدروجين الالكتات؛ البروتين التفاعلي C؛ مؤشرات حيوية تنبؤية؛ اليمن؛ مرحلة الورم؛ مستقبلات الهرمون.

How to cite this article:

N. A. N. Salem, and G. Abdul-Hamid, "SERUM FERRITIN, LDH, AND CRP AS POTENTIAL PROGNOSTIC BIOMARKERS IN BREAST CANCER: ASSOCIATION WITH TUMOR GRADE, STAGE, AND RECEPTOR STATUS", *Electron. J. Univ. Aden Basic Appl. Sci.*, vol. 7, no. 2, pp. 182-186, Jun. 2026. DOI: https://doi.org/10.47372/ejua-ba.2026.2.540