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Platelet-To-Lymphocyte Ratio in Blood in Early Breast Cancer Patients

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Abstract

Background: Breast cancer is the most prevalent malignancy among women globally and remains a leading cause of morbidity and mortality. This study aimed to assess the platelet-to-lymphocyte ratio (PLR) as a prognostic and predictive marker in early breast cancer. **Methods:** A cross-sectional study was conducted on 100 female breast cancer patients at the Haemato-Oncology Unit, Benha University Hospitals. Patients were divided into two groups based on PLR: Group I (n=57) with high PLR (>150) and Group II (n=43) with low PLR (<150). All underwent pathological evaluation, immunohistochemistry, molecular subtyping, PLR analysis, and assessment of response to neoadjuvant chemotherapy. **Results:** Tumour-node-metastasis (TNM) staging significantly differed between the two groups (P<0.001 for T, N, and M). Tumor size was significantly larger in the high PLR group both pre- and post-treatment (P=0.002, <0.001, respectively). Metastasis occurred more frequently in patients with high PLR (P<0.001). High PLR was associated with aggressive tumour features, including advanced stage, higher Ki-67 expression, HER2 positivity, and increased incidence of distant metastases. **Conclusion:** PLR is a valuable prognostic and predictive marker in early breast cancer. Elevated PLR (>150) correlates with more aggressive tumor characteristics and poorer outcomes. It may reflect a heightened systemic inflammatory response, potentially contributing to disease progression. These findings support incorporating PLR into routine clinical assessment to improve prognostication and therapeutic decision-making.

Keywords: Platelet-To-Lymphocyte Ratio; Blood; Early Breast Cancer.

Introduction

According to morbidity and mortality statistics, breast cancer is currently the most prevalent malignancy among women worldwide. Approximately 2.3 million incident cases and 0.7 million deaths were recorded worldwide in 2020, making breast cancer the most prevalent cancer and the primary cause of cancer-related fatalities among women.

By the end of 2020, a minimum of five years had elapsed since the diagnosis of breast cancer for 7.8 million women worldwide [(1)].

Egypt's cancer incidence was nearly 22,700 in 2020, and it is expected to rise to approximately 46,000 by 2050. There are 38.8% of all cancer cases in the female population, with breast cancer being the most prevalent malignancy. In terms of cancer-related mortality, breast cancer is the second most prevalent cause, with an estimated mortality rate of approximately 11%, following liver cancer [(2)].

Inflammation has a significant impact on the development and occurrence of breast cancer. The invasion, metastasis, and angiogenesis of tumor cells are intricately linked to neutrophils, monocytes, platelets, and lymphocytes in peripheral circulation [(3)].

Experimental and epidemiological research in human malignancies, such as breast cancer (BC), has indicated that platelets are essential for the progression of cancer. To facilitate the release of growth factors and adhesion molecules, as well as the degradation of the extracellular matrix and angiogenesis, the progression of the tumour requires platelet activation. Platelets enhance tumor growth and motility by shielding tumor cells from immune system attacks [(4)].

The high platelet-to-lymphocyte ratio leads to an increase in the number of platelets in circulation. Inflammatory cytokines, such as interleukin (IL)-3, IL-6, and IL-10, which are excreted by cancer cells, can promote the proliferation of megakaryocytes. The phenomenon of PLR is clarified by this hypothesis. Consequently, an increase in platelet counts is a sign of inflammation that is caused by a tumor. It is widely acknowledged that lymphocytes are responsible for the immune response against malignancies, which suggests that PLR may be linked to chemotherapy sensitivity and prognosis [(5)].

Therefore, PLR in peripheral blood is regarded as a prognostic parameter in a variety of malignancies, such as breast cancer, and is a marker of the systemic inflammatory response [(6)].

Therefore, investigating peripheral blood marker PLR in patients with breast cancer appears to be beneficial

The objective of this investigation was to assess the platelet-to-lymphocyte ratio as a prognostic indicator in the early stages

of breast cancer. Evaluating the predictive and prognostic potential of this relationship.

Patients and methods

This cross-sectional study included 100 female patients with breast cancer presented to Haemato-Oncology Unit, Benha University Hospitals from March 2023 to March 2024 (one year). An informed written consent was obtained from the patients. The purpose of the study was to explain to each patient, and they were assigned a secret code number. The research was conducted with the approval of the Research Ethics Committee at the Faculty of Medicine at Benha University.

Inclusion criteria were female patients with early primary breast cancer and histopathological confirmation of invasive breast cancer.

Exclusion criteria were Patients who were male, had a double primary cancer, metastatic breast cancer, had received treatment, had recurrent breast cancer, or had additional hematological diseases and presented with breast cancer.

Grouping: Patients were divided into equal groups regarding PLR: **Group I (n=57):** High PLR >150. **Group II (n=43):** Low PLR <150.

All studied cases were subjected to the following: Full history taking, including [Demographic Information including age, gender, ethnicity, occupation, presenting complaint including chief complaint (breast lump, pain, nipple discharge, skin changes), duration of symptoms, progression of symptoms, past medical history including history of breast cancer or other cancers, previous breast biopsies or surgeries, comorbidities, history of thrombocytopenia, thrombocytosis, or lymphopenia, family history including family history of breast cancer or other malignancies, genetic predisposition, medication history: current medications, hormonal therapies or contraceptives, chemotherapy or radiotherapy history, lifestyle and social history including smoking, alcohol consumption, and drug use, physical activity and diet, exposure to environmental carcinogens, menstrual and reproductive history including age at menarche and menopause, parity and age at first childbirth, history of breastfeeding, use of hormone replacement therapy]. **Full clinical examination: General examination including [**Vital signs (blood pressure, heart rate, respiratory rate, temperature), general appearance (e.g., pallor, lymphadenopathy), weight and BMI was calculated by dividing a person's weight in kilograms by the square of their height in meters [(7)], breast examination including inspection, palpation and systemic examination including abdominal examination and respiratory examination. **Routine laboratory investigations** [Complete blood count, including platelet count, lymphocyte count, calculation of PLR, tumor markers such as CA 15-3 and carcinoembryonic antigen, hormonal

receptor status (ER, PR, HER2, HER3-neu), inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), liver and renal function tests]. **Imaging** including breast ultrasound, CT or PET-CT. Histopathology examination of H&E-stained slides of the surgical specimen to confirm invasiveness of the neoplasm. ER, PR and HER-2 by immunohistochemical interpretation.

Pathological assessments:

Histopathological and immunohistochemistry (IHC) examinations were conducted on all surgical specimens and breast cancer biopsies from patients who had Neoadjuvant Chemotherapy (NACT) at the Chengdu Fifth People's Hospital in Sichuan, China. Haematoxylin and eosin (H&E) stained slides were analyzed to confirm the neoplasm's invasion. The nuclear grade was determined using the Nottingham grading method.

Immunohistochemical analysis: With receptor staining in 10% or more of tumour cell nuclei, the tumour was determined to be oestrogen receptor (ER) or progesterone receptor (PR) positive. To be considered HER2 positive according to the ASCO/CAP guidelines, an immunohistochemistry score of 3+ (HercepTest™, Dako Italia, Milan, Italy) and/or confirmation of HER2 gene amplification by fluorescence in situ hybridization or silver in situ hybridization (SISH) were necessary. Luminal A and luminal B malignancies were distinguished by evaluating the Ki-67 index with the MIB-1 antibody; a cutoff point of 14% was used for this purpose.

Molecular subtyping: Based on IHC and HER2 testing, tumors were categorized into molecular subtypes, including Luminal A, Luminal B/HER2-negative, Luminal B/HER2-positive, HER2-enriched, and Triple-negative.

Assessment of response to neoadjuvant chemotherapy (NACT): The clinical responses were evaluated every two cycles of NACT using the Response Evaluation Criteria in Solid Tumours (RECIST). There were two categories for the responses: partial response (PR) and non-PR. After NACT, the pathological response was evaluated by microscopically examining the removed specimens. Removing all signs of cancer from the breast and lymph nodes was considered a pathological complete response (PCR). Persistent ductal carcinoma in situ (DCIS) patients were still deemed to have attained PCR.

Platelet-to-lymphocyte ratio (PLR) analysis: Before starting therapy and again two weeks following the second NACT cycle, blood samples were taken from every patient to assess the inflammatory response. Total platelet count divided by total lymphocyte count is the formula for platelet-lymphocyte ratio (PLR). Because granulocyte colony-stimulating factor (G-CSF) is routinely administered during NACT

and may have influenced neutrophil counts, this investigation prioritized PLR over NLR. In contrast, thrombocytopoiesis agents were not used during early NACT cycles, ensuring the reliability of PLR measurements as an inflammatory marker.

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Statistical analysis

The tool SPSS v26, created by IBM© and based in Armonk, NY, USA, was used to do statistical study. Using the Shapiro-Wilks test and histograms, we could ascertain if the data had a normal distribution. The averages and standard deviations (SD) of the quantitative parametric data were assessed with an unpaired student t-test. To analyze the qualitative variables, which were given as percentages and frequencies, the suitable statistical tests were the Fissure exact test and the Chi-square test. To determine statistical significance, a two-tailed P value less than 0.05 was utilised. You can compare the meanings of two populations using the paired sample t-test when there is a correlation between two samples.

Results

Table 1 Indicated there was no significant difference between both groups regarding the age, residence and the family history of breast cancer and oral contraceptive pills, there was no significant difference between both groups regarding the platelet count and PNR. The pathological findings were insignificantly different between both groups. There was a significant difference between both groups regarding the molecular subtypes (P<0.001). Luminal A and B were significantly lower in patients with high PLR, while Her2 enriched and basal tumour were significantly higher in patients with high PLR, compared to those with low PLR.

Table 2 proved that the tumor-node-metastasis (TNM) classification before treatment, T staging was significantly different between both groups (P=0.002), while there was an insignificant difference between both groups about N and M staging. There was a significant difference between both groups regarding the tumor stages (P<0.001). The expressions of ER and PR were significantly lower in patients with higher PLR compared to those with low PLR (P=0.005, <0.001), while the expression of HER2 was significantly higher in patients with higher PLR compared to those with low PLR (P=0.012). The KI67 expression was significantly higher in patients with higher PLR compared to those with low PLR (P <0.001).

Table 3 showed the TNM classification including T, N and M staging were significantly different between both groups (P<0.001, <0.001, <0.001).

Table 4 demonstrated Before and after treatment, the tumor mass was significantly higher in patients with

higher PLR compared to those with low PLR (P=0.002, <0.001). There was a significant difference between both groups regarding the metastasis (P<0.001), as patients with high PLR >150 showed higher metastasis compared to those with low PLR.

Table 1: Demographic data, laboratory finding, pathology and molecular subtypes of the studied groups regarding PLR

		Total (n=100)	High PLR >150 (n=57)	Low PLR <150 (n=43)	P value
Demographic data					
Age (years)	**Mean± SD**	49.96± 9.13	51.26± 9.1	48.23± 8.99	0.101
	Range	32-71	32-71	37-71	
Residence	**Urban**	50 (50%)	28 (49.12%)	22 (51.16%)	0.839
	Rural	50 (50%)	29 (50.88%)	21 (48.84%)	
Family history of breast cancer		4 (4%)	4 (7.02%)	0 (0%)	0.132
OCP		43 (43%)	16 (28.07%)	27 (62.79%)	**<0.001 ***
Laboratory finding					
WBCs	**Mean± SD**	7.15± 2.88	5.8± 1.74	8.86± 3.13	**<0.001 ***
(× 10^9/L)	**Range**	3.4-13.4	3.4-9	4.4-13.4	
Platelet count	**Mean± SD**	288.71± 51.69	285.13± 44.2	293.21± 60.04	0.447
(× 10^9/L)	**Range**	225-450	230-350	225-450	
Neutrophil (%)	**Mean± SD**	4.37± 2.16	3.94± 1.72	4.93± 2.54	**0.023***
	Range	1.6-9.3	1.6-7	2-9.3	
	Median (IQR)	3.75 (2.7-5.7)	3.5 (2.7 - 5.4)	5 (2.4 - 6.5)	
Lymphocyte (%)	**Mean± SD**	2.21± 1.31	1.33± 0.33	3.36± 1.23	**<0.001 ***
	Range	0.8-6.1	0.8-1.8	2-6.1	
PLR	**Mean± SD**	168.42± 96.35	228.44± 84.1	88.87± 32.9	**<0.001 ***
	Range	12-437	156-437	12-131	
PNR	**Mean± SD**	80.77± 39.85	85.74± 37.11	74.19± 42.76	0.152
	Range	30-168	32-168	30-150	
	Median (IQR)	70 (45 – 113)	87 (64 - 113)	52 (43.5 - 120)	
	Range		0.4-1		
Pathology	**ILC**	19 (19%)	11 (19.3%)	8 (18.6%)	0.062
	IDC	77 (77%)	46 (80.7%)	31 (72.09%)	
	DCIS	4 (4%)	0 (0%)	4 (9.3%)	
Molecular subtypes	**Luminal A**	47 (47%)	19 (33.33%)	28 (65.12%)	**<0.001 ***
	Luminal B	15(15%)	3 (5.26%)	12 (27.91%)	
	Her2 enriched	18 (18%)	15 (26.32%)	3 (6.98%)	
	Basal	20 (20%)	20 (35.09%)	0 (0%)	

Data presents as Mean± SD, Range or frequency (%). OCP: oral contraceptive pills. PLR: Platelet to lymphocytic ratio, ILC: Invasive lobular carcinoma, IDC: Invasive ductal carcinoma, DCI: Ductal carcinoma in situ, PLR: Platelet to lymphocytic ratio. PLR: Platelet to lymphocytic ratio, WBCs: white blood count, PNR: platelet-to-neutrophil ratio *: statistically significant P value <0.05.

Table 2: Tumour classification (TNM) before treatment, stages, immunohistochemical findings and KI67 of the studied groups regarding PLR

		Total (n=100)	High PLR >150 (n=57)	Low PLR <150 (n=43)	P value
T	**T 1**	8 (8%)	0 (0%)	8 (18.6%)	**0.002***
	T 2	68 (68%)	41 (71.93%)	27 (62.79%)	
	T 3	20 (20%)	12 (21.05%)	8 (18.6%)	
	T 4	4 (4%)	4 (7.02%)	0 (0%)	
N	**N0**	19 (19%)	7 (12.28%)	12 (27.91%)	0.063
	N1	53 (53%)	30 (52.63%)	23 (53.49%)	
	N2	28 (28%)	20 (35.09%)	8 (18.6%)	
M	**M0**	100 (100%)	57 (100%)	43 (100%)	---
Stages	**I**	4 (4%)	0 (0%)	4 (9.3%)	**<0.001***
	IIA	15 (15%)	3 (5.26%)	12 (27.91%)	
	IIIA	32 (32%)	20 (35.09%)	12 (27.91%)	
	IIB	45 (45%)	30 (52.63%)	15 (34.88%)	
	IIIB	4 (4%)	4 (7.02%)	0 (0%)	
ER	**Positive**	73 (73%)	34 (59.65%)	39 (90.7%)	**0.005***
	Negative	27 (27%)	23 (40.35%)	4 (9.3%)	
PR	**Positive**	76 (76%)	33 (57.89%)	43 (100%)	**<0.001***
	Negative	24 (24%)	24 (42.11%)	0 (0%)	
HER2	**Positive**	18 (18%)	15 (26.32%)	3 (6.98%)	**0.012***
	Negative	82 (82%)	42 (73.68%)	40 (93.02%)	
KI67 (%)	**Mean± SD**	26.52 ± 21.53	33.25± 24.51	17.6± 12.22	**<0.001***
	Range	0-70	0-70	5-45	
	Median (IQR)	15 (12-5)	35(12-60)	14(10-15)	

Data presents as frequency (%). T: Primary tumour, N: regional lymph nodes, M: metastasis, ER: Oestrogen receptor, PR: progesterone receptor. PLR: Platelet to lymphocytic ratio, HER2: human epidermal growth factor receptor 2, ER: Oestrogen receptor, PR: progesterone receptor. PLR: Platelet to lymphocytic ratio, *: statistically significant P value <0.05.

Table 3: Tumor classification (TNM) after treatment of the studied groups regarding PLR

		Total (n=100)	High PLR >150 (n=57)	Low PLR <150 (n=43)	P value
T	**T0**	4 (4%)	0 (0%)	4 (9.3%)	**<0.001***
	T1	22 (22%)	7 (12.28%)	15 (34.88%)	
	T 1a	4 (4%)	4 (7.02%)	0 (0%)	
	T 1b	16 (16%)	4 (7.02%)	12 (27.91%)	
	T 1c	12 (12%)	4 (7.02%)	8 (18.6%)	
	T IIIA	4 (4%)	4 (7.02%)	0 (0%)	
	T2	34 (34%)	30 (52.63%)	4 (9.3%)	
	T3	4 (4%)	4 (7.02%)	0 (0%)	
N	**N0**	59 (59%)	20 (35.09%)	39 (90.7%)	**<0.001***
	N1	32 (32%)	28 (49.12%)	4 (9.3%)	
	N1c	1 (1%)	--	--	
	N2	8 (8%)	8 (14.04%)	0 (0%)	
M	**M0**	74 (74%)	35 (61.4%)	39 (90.7%)	**<0.001***
	M1	26 (26%)	22 (38.6%)	4 (9.3%)	

Data presents as frequency (%). T: Primary tumour, N: regional lymph nodes, M: metastasis, *: statistically significant P value <0.05.

Table 4: Tumor mass of the studied groups and metastasis of the studied groups regarding PLR

		Total (n=100)	High PLR >150 (n=57)	Low PLR <150 (n=43)	P value
Before	**Mean± SD**	3.62± 1.6 x 2.7± 1.54	2.71± 1.03 x 2.2± 0.76	3.23± 1.45 x 2.48± 1.29	**0.002***
	Range	1.6-7.5 x 1.1-6.3	1.4-5.2 x 1.2-4	1.4-7.5 x 1.1-6.3	
	Median (IQR)	3.2 (2.5 - 3.8) x 2.1 (1.5 - 3.7)	2.4 (2 - 3.5) x 2 (1.7 -2.5)	2.7 (2.3 - 3.7) x 2 (1.65 - 2.7)	
After	**Mean± SD**	2.52± 1.24 x 2.35± 1.48	1.42± 1.21 x 1.39± 1.16	2.04± 1.34 x 1.94± 1.43	**<0.001***
	Range	0.5-5 x 0.4-5.5	0-4.8 x 0-4.5	0-5 x 0-5.5	
	Median (IQR)	2.5 (1.6 – 3) x 1.7 (1.4- 3.5)	1.5 (0.8 - 1.6) x 1.4 (0.5 - 1.6)	1.65 (0.9 -3) x 1.5 (1 -2.5)	
Metastasis	**Brain**	4 (4%)	4 (7.02%)	0 (0%)	**<0.001***
	Liver	11 (11%)	11 (19.3%)	0 (0%)	
	Bone	7 (7%)	7 (12.28%)	0 (0%)	
	Brain & liver	4 (4%)	4 (7.02%)	0 (0%)	
	Contralateral breast	4 (4%)	4 (7.02%)	0 (0%)	
	Liver & contralateral breast	4 (4%)	0 (0%)	4 (9.3%)	

Data presents as Mean± SD, Range, Median (IQR) or frequency (%). PLR: Platelet to lymphocytic ratio, *: statistically significant P value <0.05.

Discussion

The most frequently diagnosed malignancy and the primary cause of cancer-related fatalities among women worldwide is breast cancer. The heterogeneity of breast cancer results in a highly variable prognosis for patients, despite the significant progress that has been made in the early detection, diagnosis, and management of the disease. To maximize treatment strategies and improve patient outcomes, it is essential to identify cost-effective, dependable prognostic and predictive biomarkers. Inflammation is the initiator, progression, and metastasis of a variety of malignancies, including breast cancer. Recent studies have increasingly focused on hematological markers derived from routine complete blood counts as potential indicators of systemic inflammation and immune response. Among these markers, the PLR has emerged as a promising prognostic indicator in different types of cancer, including breast cancer [8].

The demographic data of the patients in the present study revealed a range of ages, from 32 to 71 years, with a mean of 49.96± 9.13 years. Fifty percent of the patients were from rural regions, while fifty percent were from metropolitan areas. Among the studied patients, 4 (4%) patients had family history of breast cancer, and there were 43 (43%) patients who received OCP.

Our results in consistent with Dan et al.,[9] who endeavoured to evaluate the predictive value of early alterations in PLR observed before and after two regimens of NACT in breast cancer patients as indicators of neoadjuvant

chemotherapy response and PCR. This retrospective research examined the data of 257 individuals who were initially diagnosed with breast cancer. The median age of the sample cohort was 50 years, with a range of 34–70 years. The distribution of individuals older than 50 years (52.1%) and younger than 50 years (47.9%) was even. Regarding menopausal status, 60.7% of patients were postmenopausal, while 39.3% were premenopausal.

The laboratory findings showed that the WBCs count of the patients studied ranged from 3.4 to 13.4 × 109/L with a mean of 7.15± 2.88 × 109/L. The platelet count ranged from 225 to 450 × 109/L with a mean of 288.71± 51.69 × 109/L. The neutrophil % ranged from 1.6 to 9.3 % with a mean of 4.37± 2.16 %. The lymphocyte % ranged from 0.8 to 6.1% with a mean of 2.21± 1.31%. The PLR ranged from 12 to 437 % with a mean of 168.42± 96.35%. The PNR of the patients studied ranged from 30-168% with a mean of 80.77± 39.85%. Serum creatinine level ranged from 0.4 to 1 mg/dL with a mean of 0.63± 0.16 mg/dL.

Our results in consistent with Ayan et al., [10] who reported that mean leukocyte count was 6.74 $\times 10^3$/mL, mean platelet count was 247.50 $\times 10^3$/mL, median neutrophil count was 3.78 $\times 10^3$/mL, median lymphocyte count was 2.20 $\times 10^3$/mL, median NLR was 1.63, and median PLR was 111.26.

Concerning the pathology, 19 (19%) patients had ILC, 77 (77%) patients had IDC, and 4 (4%) patients had DCI. Among the studied patients, 47 (47%) patients had luminal A tumor, 15(15%) patients had luminal B tumor, 18 (18%) patients had Her2 enriched tumor, and 20 (20%) patients had tumor.

Our results in concordance with Dan et al., [9] revealed that the most frequent molecular subtype was Luminal A, accounting for 44.1% of cases. This subtype is typically associated with a favorable prognosis and good response to hormonal therapy due to its hormone receptor positivity and low proliferation index. HER2-enriched subtypes comprising 23.3% of the population. Luminal B subtype was the least common, making up 9.3% of cases.

In contrast, Ma et al., [11] who conducted research on the effect of PLR on the complete pathological response (PCR) of breast cancer patients following neoadjuvant chemotherapy (NAC).The scope of this investigation included 112 patients with malignant melanoma. In the PCR group, HER-2 enriched (42.1%, 24 out of 57) and Luminal B (HER-2 positive) (43.9%, 25 out of 57) subtypes were the most common molecular classifications, collectively comprising over 85% of PCR cases.

Regarding the tumor classification before treatment, 8 (8%) patients were classified as T1, 68 (68%) patients were classified as T2, 20 (20%) patients were classified as T3, and 4 (4%) patients were classified as T4. Additionally, 19 (19%) patients were classified as N0, 53 (53%) patients were classified as N1, and 28 (28%) patients were classified as N2. All patients were classified as M0. Concerning the tumor staging, 4 (4%) patients were stage I, 15 (15%) patients were stage IIA, 32 (32%) patients were stage IIIA, 45 (45%) patients were stage IIB, and 4 (4%) patients represented stage IIIB. The immunohistochemical analysis showed that 73 (73%) patients

had positive ER, 76 (76%) patients had positive PR, and 18 (18%) patients had positive HER2.

Our results in concordance Wang et al., [12] demonstrated that in this cohort of breast cancer patients, the majority presented with early-stage disease, with T1 tumors accounting for 57.8% and Stage II disease comprising 56.6%, reflecting a relatively favorable tumor burden at diagnosis. Regarding hormone receptor status, estrogen receptor (ER) positivity was high (72.3%), while PR positivity was seen in 62.0%, consistent with a predominance of hormone-responsive tumors. HER2 positivity was noted in 40.4%, indicating a significant subset that may benefit from targeted anti-HER2 therapies. Additionally, N0 nodal status was observed in 62.7%, and only 15.1% showed suspicious lymph nodes on ultrasonography, further supporting early-stage detection in many patients.

In contrast to a study by Krenn-Pilko et al., [13] found that most patients presented with early-stage tumors, with T1 tumors comprising 56.7% of cases. However, a significant proportion (22.4%) had T2 tumors, and 12.9% had T3 tumors, while advanced local disease (T4) was present in 4.8%, reflecting a subset of patients still diagnosed at later stages. Regarding lymph node involvement, 57.3% were node-negative (N0), which correlates well with the high proportion of T1 tumors. However, N1 and N2 nodal disease made up a notable 36.1%, indicating regional spread in over one-third of patients, and N3 disease in 5.7% suggests a more advanced nodal burden in a small subgroup.

In our study we found that the KI67 expression of the studied patients ranged from 0 to 70 % with a mean of 26.52 ± 21.53% and a median (IQR) of 15 (12-5) %.

Our results in consistent with Wang et al., [12] demonstrated that a higher proliferation index (Ki-67 >20%) was found in 56.6% of cases, suggesting that a significant proportion of tumors exhibited more aggressive biological behavior.

In the current study, we observed that 57 (57%) patients had a high PLR >150, while 43 (43%) patients had a low PLR <150. Furthermore, patients with a high PLR >150 exhibited significantly lower OCP consumption than those with a low PLR <150 (P<0.001). There was no significant difference between the two groups in terms of the age, domicile, and family history of breast cancer and oral contraceptive medications. The pathological findings were insignifcantly different between both groups.

Our results in consistent with Lu et al., [14] the purpose of which was to evaluate the prognostic significance of the combination of pre-treatment NLR, PLR, and PD-L1 in breast cancer. Overall, 870 patients diagnosed with breast cancer were included in the study. The median age of patients with low and high PLR was not statistically significantly different, suggesting that PLR levels are not age dependent.

In the laboratory, patients with a high PLR >150 exhibited a significantly lower WBC count, neutrophil, and lymphocyte count compared to those with a low PLR <150 group (P <0.001, 0.023, <0.001), whereas patients with a high PLR >150 exhibited a significantly higher PLR (P <0.001, <0.001). The platelet count and PNR did not exhibit

any significant differences between the two groups.

Our results in consistent with Huszno et al., [15] The researchers discovered that individuals with a high PLR (PLR >89.6) exhibited significantly lower WBC (6.16×10^9/L vs. 7.45×10^9/L, P=0.0009) and lymphocyte counts (1.75×10^9/L vs. 2.44×10^9/L, P=0.0001) than those with a low PLR (PLR ≤89.6). In addition, the high PLR group exhibited a higher platelet count (230×10^9/L vs. 165×10^9/L, P=0.0001) and an elevated NLR (2.08 vs. 1.66, P=0.002).

It was discovered in the present investigation that the molecular subtypes of both groups differed significantly (P<0.001). In comparison to patients with low PLR, those with high PLR exhibited significantly lower levels of luminal A and B, as well as significantly higher levels of Her2 enriched and basal tumor.

This came in accordance with Tekyol et al., [16] examining inflammatory biomarkers in breast cancer patients found that HER-2 enriched tumors had a higher prevalence in patients with high PLR (≥150), while Luminal A tumors were more common in those with low PLR (<150).

When it comes to the TNM classification prior to treatment, the T staging was significantly different between the two groups (P=0.002), whereas the N and M staging did not differ significantly between the two groups. The tumor phases of both groups were significantly different (P<0.001).

Similarly, our findings in agreement with Gong et al., [8] A significant correlation was found between an advanced TNM stage and a high PLR (OR = 1.89; 95% CI 1.25, 2.87; P = 0.003; I2 = 84%; P < 0.01).

Also, our findings in line with Lu et al., [17] determined that analysis of tumor stage distribution between the low and high PLR groups revealed a statistically significant difference (P = 0.044). These findings suggest that a higher PLR may be associated with more advanced disease at presentation, supporting its role as a potential indicator of tumor aggressiveness.

Patients with a higher PLR exhibited significantly lower expressions of ER and PR compared to those with a low PLR (P=0.005, <0.001). Conversely, patients with a higher PLR exhibited significantly higher expression of HER2 (P=0.012).

This came in accordance with Krenn-Pilko et al., [13] found that a high PLR significantly correlated with ER-negative tumors, PR status and Her2 overexpression.

In disagreement with the present study, Lu et al., [17] The low and high PLR groups did not exhibit any statistically significant differences in terms of ER, PR, and HER2. This was determined.

In comparison to patients with low PLR, the present investigation demonstrated that the KI67 expression was significantly higher in patients with higher PLR (P <0.001).

Our findings in agreement with Bahgat, T. [18] found that a statistically significant association was observed between Ki-67 expression levels and PLR groups (P = 0.001). Specifically, the high Ki-67

(>14%) was markedly more frequent in the high PLR group (90%) compared to the low PLR group (37.5%). Conversely, low Ki-67 (<14%) was more common in the low PLR group (62.5%).

In contrast, our findings disagreed with Asano et al., [19] According to the report, 52.2% of the low PLR group and 61.8% of the high PLR group exhibited Ki-67 levels exceeding 14%, which are indicative of increased tumor proliferation. Even though a greater number of patients in the high PLR group manifested elevated Ki-67 levels, the difference did not reach statistical significance (P = 0.210).

In the present investigation, we found that the TNM classification, which includes T, N, and M staging, differed significantly between the two groups (P<0.001, <0.001, <0.001). Both before and after treatment, patients with a higher PLR had a significantly larger tumor mass than those with a low PLR (P=0.002, <0.001).

Our results in consistent with Anwar et al., [20] showed that the tumor mass was significantly higher in patients with higher PLR compared to those with low PLR.

The present study revealed that there was a significant difference between both groups regarding the metastasis (P<0.001), as patients with high PLR >150 showed higher metastasis compared to those with low PLR.

As well, our results in concordance with Gong et al., [8] In breast cancer patients with lymph node metastasis (OR = 1.82; 95% CI 1.32, 2.52; P < 0.001), advanced TNM stage (OR = 1.89; 95% CI 1.25, 2.87; P = 0.003), and distant metastasis (OR = 1.76; 95% CI 1.14, 2.72; P = 0.01), elevated PLR was observed.

The limitations of the study were that this study was limited by its cross-sectional design, which does not allow assessment of long-term outcomes such as overall survival or disease-free survival, the sample size was relatively small and conducted at a single center, which may limit the generalizability of the results and PLR was measured at a single time point, without accounting for changes over time or after treatment.

Conclusion

Early breast cancer patients exhibit a significant prognostic and predictive marker known as PLR. Tumour characteristics that were more aggressive were significantly correlated with a high PLR (>150), including a higher tumour size and stage, increased Ki67 expression, HER2 positivity, and a higher incidence of distal metastases. Additionally, patients with high PLR were more likely to have unfavorable molecular subtypes, such as HER2-enriched and basal-like tumors, and showed lower expression of hormone receptors (ER and PR). These findings suggest that PLR reflects the systemic inflammatory response and may play a role in breast cancer progression. Given its simplicity, cost-effectiveness, and accessibility, PLR could serve as a useful tool in routine clinical practice for risk stratification and tailoring treatment strategies in patients with early breast cancer.

As a result, PLR should be considered a routine and cost-effective marker that can be employed to assess the prognosis of patients with early breast cancer. It is advised that larger multicenter studies be

conducted with extended follow-up periods to verify these findings and evaluate the correlation between PLR and long-term outcomes, including disease-free and overall survival. To improve risk stratification and treatment planning in breast cancer, future research should explore the incorporation of PLR with other clinical and pathological markers.

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