Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

ORIGINAL RESEARCH

Association of NLR PLR RDW in Breast Cancer Patients

[1]Dr. Akshai M.U., [2]Dr. Anup Paul Varkey, [3]Dr. Aneesh Raj A., [4]Dr. Maheshwaran M.P.

[1]Senior Resident, [2,3]Assistant Professor, Department of Surgery, Government Medical College, Alappuzha, Kerala, India.
[4]Assistant Professor, Department of General Surgery, Government Medical College, Alappuzha, Kerala, India.

Corresponding author
Dr. Maheshwaran M.P.
Assistant Professor, Department of General Surgery, Government Medical College, Alappuzha, Kerala, India.

Received: 16 March, 2023 Accepted: 19 May, 2023

Abstract

Background: Breast cancer is the most frequently diagnosed life-threatening cancer in women in India. The short-term and long-term prognosis of breast cancer depends upon patient and tumor factors, such as age, disease stage, and biological factors such as grade and receptor status. However, the behavior of breast cancer is unpredictable, with markedly different clinical outcomes seen even among patients with similar classical prognostic factors. The significance of neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio(PLR) and red cell distribution width (RDW)as inflammatory marker has been increasing. In this study, we try to find out NLR, PLR, RDW values in patients with carcinoma breast and to study its association with various biological features of cancer breast like stage, Modified Bloom Richardson (MBR) grade, hormonal status(ER-estrogen receptor, PR-progesterone receptor, HER2NEU-herceptin receptor) and age of the patient.

Methods: This was a longitudinal study conducted in General Surgery Department of a tertiary care centre in South India . All patients admitted to the hospital with histologically and radiologically proven diagnosis of carcinoma breast during December 2019 to November 2020 were included in the study. The sample size was calculated to be 100 patients. Blood sample were collected from these patients as part of routine workup and were analysed. Data was entered into Microsoft excel data sheet and was analyzed using SPSS for Windows (Statistical Presentation System Software, SPSS Inc.) version 17.0.

Results: We studied 100 patients diagnosed with carcinoma breast. The mean age in the study group was 54.17. Based on the Modified Bloom Richardson (MBR) criteria all patients were categorised into three grades-I, II & III. 40 patients were categorised into grade II, were as 29 were in grade I. Cut off value for NLR was placed as </=3,& majority of the patients with high MBR & tumor grade comes 69.2 %, of grade 3 showed high NLR. For PLR there is a significant difference ($p<0.001$) in </=200 and >200 between MBR grade I, II, &III. in</=200 group majority of the participants (50%) were in MBR grade II and in >200 all of the participants (100%) were in MBR grade III, which was statistically significant. RDW, there is a significant difference ($p<0.001$) in </=14.2 and >14.2 between MBR grade I, II, &III. in</=14.2 group majority of the participants (51.4%) were in MBR grade II and in >14.2 majority of the participants (83.3%) were in MBR grade III.

Conclusion: NLR, PLR & RDW are very productive and easily available from routine haemogram test. It helps to analyze the various stages in breast cancer and its relation to

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

different stages of breast cancer and based on pathological grading we could be vigilant before going to the definitive treatment on Ca breast. Higher the NLR, PLR, RDW values, the patient should be further evaluated for metastasis and disease progression.

Keywords: neutrophil –lymphocyte ratio(NLR), platelet- lymphocyte ratio(PLR), red cell distribution width(RDW), modified bloom Richardson grade(MBR), carcinoma breast.

Introduction

Cancer is the second leading cause of death worldwide after cardiovascular diseases.[1]Breast cancer is the most frequently diagnosed life-threatening cancer in women including in India.[2] Cervical cancer was the most common cancer in women in India for decades, and more deaths in women in India were attributed to cervical cancer than any other cancer.[3] But over the last 10 years or so, breast cancer has been rising steadily, and for the first time in 2012, breast cancer was the most common cancer in women in India, a way ahead of cervical cancer.[2,4,5] Newly diagnosed Indian patients account for 17.7% of those all over the world.[6] Breast cancer has the highest crude incidence rate and mortality among all cancer types in Kerala.[7] The short-term and long-term prognosis of breast cancer depends upon patient and tumor factors, such as age, disease stage, and biological factors such as grade and receptor status. However, the behavior of breast cancer is unpredictable, with markedly different clinical outcomes seen even amongst patients with similar classical prognostic factors.[8] Inflammatory cells and mediators in the tumor microenvironment are thought to play an important role in cancer progression, and may account for some of this variability. The prognostic factors of breast cancer include lymph node status, tumor size, histological type, histological grade, lymphatic–vascular invasion[9] HER2 (human epidermal growth factor receptor 2) over-expression has also been shown to be a significant predictive and prognostic factor in the presence of estrogen (ER) and progesterone (PR) expression.[10] Cancer related inflammation is now considered as an effective marker in cancer prognosis. The host leukocytes, particularly tumour-associated macrophages (TAM) in the microenvironment of the neoplastic tissue, play a key role. The transcription factors(such as nuclear factor-kB [NF-kB], signal transducer and activator of transcription-3 [Stat3]), cytokines (such as TNF, IL-1, IL-6), and chemokines (such as CCL2 and CXCL8) released from tumour cells and the leukocytes in this microenvironment lead to tumour angiogenesis, tumourcell survival, and proliferation.[11]The inflammation markers with prognostic significance in patients with cancer include C-reactive protein[12] and abnormal inflammation-based score (Glasgow Prognostic Score, GPS).[13] The significance of neutrophil to-lymphocyte ratio (NLR) as an inflammation marker has been increasing. The production and release of neutrophils increases in the bone marrow in response to inflammation. The chemokines playing a significant role in cancer-related inflammation induce neutrophil release from the bone marrow resulting in accumulation of neutrophils in peripheral tissue.[14] NF-kB activates human neutrophils and prolongs neutrophil survival.[15] In-vivo studies have shown that IL-1 induces neutrophil sequestration by regulating chemokine expression.[16] In contrast to such an effect on neutrophils, inflammation shows an inverse effect on lymphocyte count due to cytokines, particularly TNF∞ and IL-1b.[17] Similarly, the CXXL2 and stem cell factors induced by the inflammation lead to granulopoiesis and inhibit lymphoid development.[12] Due to all these effects of inflammation, the neutrophil count increases while lymphocyte count decreases in peripheral blood. Consequently, these changes increase the NLR. Since increased NLR may be a marker of cancer related inflammation, it may also be associated with prognosis. Several studies have shown that high NLR may be associated with poor prognosis in various types of cancer.[18] However, there are limited studies in the literature demonstrating the prognostic significance of NLR in breast cancer. Furthermore, a prognostic significance similar to that of NLR has been shown for derivedNLR (dNLR) defined as the

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

neutrophil count to white cell count–neutrophil count.[19] Defining this new ratio was intended to be a way to record the lymphocyte count while recording routine treatment data of cancer patients who are not part of a study. Red cell distribution width (RDW) is a measurement of variability and size of erythrocytes, and is performed routinely as part of a complete blood cell count. As an easy-to-measure inflammatory marker of systemic inflammatory response, RDW has been reported in many patho-physiological conditions including cardiovascular disease and generally increased progressive inflammations.[20]Recently, RDW is increasingly being recognized to have an important role in carcinogenesis, tumour progression and prognosis.[21]

Materials &methods

This study was conducted in the department of general surgery at Government Medical College Alappuzha, India. The sample size of a minimum of 100 patients fulfilling the inclusion criteria waspart of this study conducted from December 2019 to November 2020. Data were collected from patients admitted in surgery wards of Alappuzha Medical College, Kerala, India, with a diagnosis of carcinoma breast proven histologically and radiologically. Blood sample were collectedfrom these patients as part of routine workup and were analysed. The study variables analysed were NLR, PLR, RDW and it association with tumor, tumor invasion, ER, PR, HER2NEU status, NACT(neo adjuvant chemotherapy).

Inclusion criteria

All patients admitted to the hospital with histologically and radiologically proven diagnosis of carcinoma breast

Exclusion criteria

Patients with Ca breast having fever, any features of inflammation, anaemia at the time of blood collection were excluded from the study.

Data was entered into Microsoft excel data sheet and was analyzed using SPSS for Windows (Statistical Presentation System Software, SPSS Inc.) version 17.0.

Continuous data was represented as mean and standard deviation. One Way ANOVA was used to compare between more than two unpaired data. Count data was represented as numbers and proportions. Chi square test was used.

Graphical representation of data

MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Pie diagram. **p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Result

Group	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	23.00	79.00	54.17	10.72
HB	100	10.00	14.60	11.79	0.97
TC	100	6500.00	17600.00	8904.30	1417.98
NEUTROPHIL	100	3360.00	15768.00	6297.98	1746.57
PLATELET	100	179000.00	480000.00	340305.00	61754.24
LYMPHOCYTES	100	951.20	4248.00	2354.58	769.19
NLR	100	1.03	14.37	3.22	2.09
PLR	100	90.58	256.20	156.11	42.32
RDW	100	12.00	17.80	13.84	1.28

Table 1. Descriptive Details

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

This study enrolled 100 patient. The minimum age was 23 and maximum age was 79. The mean age was 54.17. Routine blood was collected and neutrophil, platelet and lymphocytes and RDW were analyzed. The minimum neutrophil count was 60 were as the maximum was 15768, the mean being 6297.98.

		Frequency	Percent
Menopause	NO	25	25.0
	YES	75	75.0
MBR GRADE	I	29	29.0
	II	40	40.0
	III	31	31.0
Type	DUCTAL	89	89.0
	LOBULAR	11	11.0
Invasion	ABSENT	20	20.0
	PRESENT	80	80.0
ER	NEGATIVE	22	22.0
	POSITIVE	78	78.0
PR	NEGATIVE	22	22.0
	POSITIVE	78	78.0
HER2NEU	NEGATIVE	82	82.0
	POSITIVE	18	18.0
NACT	NO	95	95.0
	YES	5	5.0
NLR	</=3	61	61.0
	>3	39	39.0
PLR	</=200	80	80.0
	>200	20	20.0
RDW	</=14.2	70	70.0
	>14.2	30	30.0

Table 2.

Of the 100 patients In the study 75 had attained menopause. Among the 100 patients 40 were having MBR II, were as 29 patients had MBR grade I. 89% of patients were having a ductal type of carcinoma. 80 patients histopathology showed invasion. 78% of patient showed ER, PR positive hormonal status, were as 18% patients were HER2neu positive. 5 patients received neo- adjuvant chemotherapy. The NLR, PLR, RDW median cutoff was calculated to be 3, 200, 14.2. 61% patients had NLR </=3, 80% had PLR </= 200, and 70% of them had RDW, </=14.2.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

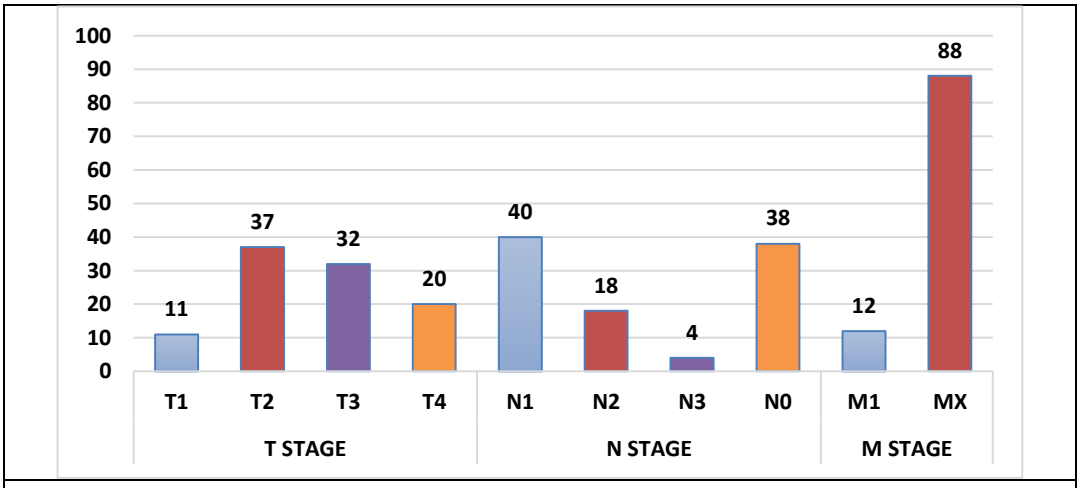

Figure 1.

The above figure shows the frequency representation of the TNM staging. Most of the patients had a T2 lesion(37%), were as 32% patients had a T3 lesion. Only 11% patients presented with T1 lesion. 20% of the patient had a T4 lesion. When considering the Nodal status 40% of patient had a N1 lesion, 8% of them had no lymph nodes (N0), 4% presented with N3 status were as 18% had N2 lesion. Out of the hundred patients 12 were found to have metastasis.

Variable	MBR grade	N	Mean	Std. Deviation	Std. Error Mean	P-value
NEUTROPHIL	I	29	5319.55	1064.05	197.59	0.001*
	II	40	5995.05	1155.80	182.75	
	III	31	7604.16	2112.47	379.41	
PLATELET	I	29	357234.4	50141.89	9311.12	0.051
	II	40	344212.5	67732.97	10709.52	
	III	31	319425.8	59382.44	10665.40	
LYMPHOCYTES	I	29	3045.48	504.30	93.65	0.001*
	II	40	2435.70	630.46	99.68	
	III	31	1603.59	381.31	68.48	

Table 3.

*Significant at the 0.05 level

Table III showed that there is no significant difference (p=0.051) in platelet between MBR grade I, II, &III. The study showed that there is significant difference (p<0.001) in neutrophil between MBR grade I, II, &III, with Grade III having the highest and Grade I with lowest neutrophil values. Lymphocytes also showed a significant difference (p<0.001) between MBR grade I, II, &III, with Grade I having the highest and Grade III with lowest LYMPHOCYTES values.

Variable	MBRgrade	N	Mean	Std. Deviation	Std. Error Mean	P-value
NLR	I	29	1.83	0.65	0.12	0.001*
	II	40	2.73	1.29	0.20	
	III	31	5.16	2.42	0.44	
PLR	I	29	119.63	16.54	3.07	0.001*
	II	40	145.00	21.48	3.40	
	III	31	204.59	34.26	6.15	
RDW	I	29	12.84	0.66	0.12	0.001*
	II	40	13.55	0.83	0.13	

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

	III	31	15.15	1.13	0.20	

Table 4.

***Significant at the 0.05 level.**

Table IV showed that there is a significant difference (p<0.001) in NLR between MBR grade I, II, &III, with Grade III having the highest and Grade I with lowest NLR values. The same was applicable for PLR and RDW. PLR showed a significant difference (p<0.001) between MBR grade I, II, &III, with Grade III having the highest and Grade I with lowest PLR values. Considering RDW, the study showed a significant difference (p<0.001) in RDW between MBR grade I, II, &III, with Grade III having the highest and Grade I with lowest RDW values.

			MBR GRADE			P-value
			I	II	III	
NLR	</=3	N	27	30	4	0.001*
		%	44.3%	49.2%	6.6%	
	>3	N	2	10	27	
		%	5.1%	25.6%	69.2%	
PLR	</=200	N	29	40	11	0.001*
		%	36.2%	50.0%	13.8%	
	>200	N	0	0	20	
		%	0.0%	0.0%	100.0%	
RDW	</=14.2	N	28	36	6	0.001*
		%	40.0%	51.4%	8.6%	
	>14.2	N	1	4	25	
		%	3.3%	13.3%	83.3%	

Table 5.

*Significant at the 0.05 level

This table shows NLR, there is a significant difference (p<0.001) in </=3 and >3 between MBR grade I, II, &III. In </=3 group majority of the participants (49.2%) were in MBR grade II and in >3 majority of the participants (69.2%) were in MBR grade III. PLR shows a significant difference (p<0.001) in </=200 and >200 between MBR grade I, II, &III. In </=200 group majority of the participants (50%) were in MBR grade II and in >200 all of the participants (100%) were in MBR grade III. RDW shows a significant difference (p<0.001) in </=14.2 and >14.2 between MBR grade I, II, &III. In </=14.2 group majority of the participants (51.4%) were in MBR grade II and in >14.2 majority of the participants (83.3%) were in MBR grade III.

			MBR GRADE			P-value
			I	II	III	
INVASION	ABSENT	N	20	0	0	0.001*
		%	100.0%	0.0%	0.0%	
	PRESENT	N	9	40	31	
		%	11.2%	50.0%	38.8%	
ER	NEGATIVE	N	1	7	14	0.001*
		%	4.5%	31.8%	63.6%	
	POSITIVE	N	28	33	17	
		%	35.9%	42.3%	21.8%	

Table 6.

*Significant at the 0.05 level

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

The table VI showed for invasion of tumour type, there is a significant difference (p<0.001) in absent and present between MBR grade I, II & III. In group were invasion was absent majority of the participants (100%) were in MBR grade I were as in the group were invasion was present majority of the participants (50%) were in MBR grade II. For the ER status there was a significant difference (p<0.001) in negative and positive groups between MBR grade I, II & III. In ER negative group majority of the participants (63.6%) were in MBR grade III and in ER positive group majority of the participants (42.3%) were in MBR grade II.

			MBR GRADE			P-value
			I	II	III	
PR	NEGATIVE	N	1	7	14	0.001*
		%	4.5%	31.8%	63.6%	
	POSITIVE	N	28	33	17	
		%	35.9%	42.3%	21.8%	
HER2NE	NEGATIVE	N	27	33	22	0.083
		%	32.9%	40.2%	26.8%	
	POSITIVE	N	2	7	9	
		%	11.1%	38.9%	50.0%	
NACT	NO	N	29	39	27	0.047*
		%	30.5%	41.1%	28.4%	
	YES	N	0	1	4	
		%	0.0%	20.0%	80.0%	

Table 7.

*Significant at the 0.05 level

Table VII states that there is no significant difference (p=0.083) in HER2NEU between MBR grade I, II, &III. But for the PR hormone status there is a significant difference (p<0.001) in the negative and positive group between MBR grade I, II & III. In the PR negative group majority of the participants (40.2%) were in MBR grade II and in PR positive group majority of the participants (50%) were in MBR grade III.

NACT(neo adjuvant chemotherapy) showed there is a significant difference (p=0.047) in the NACT negative and NACT positive groups between MBR grade I, II & III. In NACT negative group majority of the participants (41.1%) were in MBR grade II were as in the group that had NACT majority of the participants (80%) were in MBR grade III.

			NLR		P value
			</=3	>3	
PR	NEGATIVE	N	7	15	0.001*
		%	11.5%	38.5%	
	POSITIVE	N	54	24	
		%	88.5%	61.5%	
HER2NE	NEGATIVE	N	54	28	0.034*
		%	88.5%	71.8%	
	POSITIVE	N	7	11	
		%	11.5%	28.2%	
NACT	NO	N	61	34	0.001*
		%	100.0%	87.2%	
	YES	N	0	5	
		%	0.0%	12.8%	

Table 8.

*Significant at the 0.05 level using Chi square test

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

Table VIII showed that the is a significant difference between PR negative hormonal status and NLR. POST NACT also showed significant association with NLR but the HER2NEU receptor status had no significant difference with NLR.

			PLR		P value
			</=200	>200	
PR	NEGATIVE	N	12	10	0.001*
		%	15.0%	50.0%	
	POSITIVE	N	68	10	
		%	85.0%	50.0%	
HER2NE	NEGATIVE	N	69	13	0.027*
		%	86.2%	65.0%	
	POSITIVE	N	11	7	
		%	13.8%	35.0%	
NACT	NO	N	79	16	0.001*
		%	98.8%	80.0%	
	YES	N	1	4	
		%	1.2%	20.0%	
Table 9.					
*Significant at the 0.05 level using Chi square test					

Table IX found out that there is significant difference between PLR and PR negative hormone status. Post NACT also showed significant association with PLR. The HER2NEU status showed no significant difference with PLR.

Discussion

This longitudinalstudy was conducted as part of post graduate training in general surgery. It was done in Government medical college Alappuzha with study titled as an ASSOCIATION OF NLR PLR RDW IN VARIOUS STAGE OF BREAST CANCER with the object of finding the association of NLR, PLR, RDW in various stages of breast cancer and to know whether it predicts the outcome of staging and its management. A total of 100 patients were enrolled and analysed from December 2019 to November 2020.

In our study the minimum age was 23 and maximum 79 with mean age 54.17 of which 75 attained menopause. Cancer-related inflammation has been shown to have adverse effects on cancer prognosis. Therefore, the high NLR resulting from inflammation is considered to be potentially related to poor prognosis and this association has been shown in a study conducted by Wu L and et al [(22)]Absolute neutrophil and lymphocyte counts could be affected by various physiological, pathological, and physical factors while NLR remains stable with respect to these factors. This is why the stability of NLR is superior to the leukocyte subtype [(19)]. NLR is an independent significant predictor of all-cause short-and long-term mortality in breast cancer patients, even after adjusting for possible confounders as studied by Azab B and et al..[(23)] Cut off value for NLR was placed as </=3, and majority of the patients(69.2%) with high MBR and tumour grade 3 showed high NLR. There was no change in NLR ratio with type & menopause, there was significant result of 97.4 % vs 68.9% for invasion(p value 0.001). For patients with ER negative PR negative NLR was more with 38.5% vs 11.5%, but there are no significance with HER2Neu. Patients who had NACT(Neo adjuvant chemo-therapy) were having high NLR values.

Various studies have shown that platelets can promote tumor-cell trans-endothelial migration and metastasis through the mediation of P2Y2 receptor. (24) Platelets can secrete a variety of

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

growth factors including platelet derived growth factor (PDGF), [25] platelet-activating factor (PAF), and vascular endothelium growth factor (VEGF), which could further support tumor growth, angiogenesis and metastasis .[26] Therefore, increased platelet counts have negative effects on patient survival. On the other hand, lymphocytes play an important role in tumor-derived inflammatory responses.[27] Lymphocytes have an antitumor activity by inducing cytotoxic cell death and inhibiting tumor proliferation. Several studies have reported that the increased infiltration of lymphocytes in tumor tissue predicted better survival outcomes in cancer patients. Notably, previous studies showed that high PLR was in association with poor survival in other tumors including non-small cell lung cancer [28]colorectal cancer [29], gastric cancer [30], and various solid tumor [31] by performing meta-analysis.

In the present study group, PLR showed that there is a significant difference ($p<0.001$) in </=200 and >200 between MBR grade I, II, &III. In</=200 group majority of the participants (50%) were in MBR grade II and in >200 all of the participants (100%) were in MBR grade Ill which was statistically significant. There was no association with invasion with PLR (p value 0.012). ER negative PR negative patient had significant high PLR 50% VS 15%. This study showed that PLR has no significance with Her2neu receptor status.

The present study suggested that elevated preoperative RDW was associated with high grade and invasive carcinoma. Also, considering that RDW is an easily available and inexpensive parameter in blood routine examination. The RDW could be a new accurate and reproducible detected index to distinguish breast cancer patients with poorer prognosis. Huang D P and et al. also explored the relationship between red cell distribution width and prognosis in patients with breast cancer.[32] The present study gives more accurate estimation about the role of RDW in the prognosis of patients with breast cancer. As a routinely available index of the systemic inflammatory response, RDW has been suggested to be associated with adverse outcomes in different cancer patients. Warwick.R and et al. found RDW is a significant factor after risk adjustment, determining in-hospital morbidity, mortality and long-term survival in patients post-potentially curative resections for non-small-cell lung cancer.[33]Albayrak et al. investigated the utility of RDW as a simple and readily available marker in prostate cancer, as well as to evaluate RDW as a predictor of progression in prostate cancer patients.[34] They reported that the mean RDW value of prostate cancer patients was 14.6, compared with 13.7 in the healthy control group (P=0.001). A higher RDW was associated with an increased risk of progression, where as a lower RDW value was correlated with a low risk of progression. But this is a study with small sample size including 62 newly diagnosed patients and 62 healthy controls. In parallel with two studies above, Kust et al. assessed clinical and prognostic value of RDW in patients with colorectal cancer[35].

The RDW not only had adverse influences on long-term outcomes, but even short-term outcomes. Yazici et al. investigated the role of red cell distribution width in predicting prognosis in gastric cancer patients[36]. They found that preoperative RDW levels were significantly higher in patients with short-term mortality (17.9 +/- 4.3 vs 16 +/- 3.2,P=0.015). In high RDW group, the incidence of advanced gastric cancer was significantly higher (75 vs 51%,P=0.002), whereas DFS (0.035) and OS (P=0.04) were lower. These results indicated that the frequency of advanced cancer was high in patients with high RDW values. High RDW values were strongly associated with short-term mortality as studied by Giralt J et al .[37] Our data supported the role of RDW in the poor prognosis for breast cancer patients. These studies suggested that RDW is an important biomarker in cancers. The mechanism that could explain the relation between RDW and survival or disease activity is not clear, but it is considered that high RDW is caused by chronic inflammation, poor nutritional status, oxidative stress, and age-related diseases that lead to changes in erythropoiesis.[38] As we all know that inflammation in the tumor microenvironment promotes tumor growth, invasion, angiogenesis, and eventually metastasis. Elevated inflammatory marker such as CRP,

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

neutrophil to lymphocyte ratio, interleukin-6, have been related to poorer survival amongst breast cancer patients.[39,40] The inflammation leads to changes in red blood cell maturation by disturbing the red cell membrane, inducing increased RDW. This may be one of the mechanisms. Our study found that higher RDW values, with larger primary tumor was significantly associated with the number of axillary lymph node metastasis. A reasonable explanation is a malignant tumor may extend the inflammatory response in the process of its progress time and increases the circulation cytokine levels. RDW may be potential biomarkers of cancer growth and metastasis activity. Another reason could be oxidative stress. Both endogenous and exogenous sources of reactive oxygen species result in increased oxidative stress in the cell. Excess reactive oxygen formed can result in damageand modification of cellular macromolecules most importantly genomic DNA that can produce mutations. In addition, oxidative stress modulates gene expression of downstream targets involved in DNA repair, cell proliferation and antioxidants. The modulation of gene expression by oxidative stress occurs in part through activation or inhibition of transcription factors and second messengers. The role of single nuclear polymorphism for oxidative DNA repair and enzymatic antioxidants are important in determining potential human cancer risk. Wan J et al reported that elevated red cell distribution width level is associated with oxidative stress and inflammation in a canine model of rapid atrial pacing, just like inflammation, the status of oxidative stress may reduce RBC survival and lead to elevated levels of RDW [41]
In our study it was found that there is a significant difference when RDW ($p<0.001$) is </=14.2 and >14.2 between MBR grade I, II, &III. In the </=14.2 group majority of the participants (51.4%) were in MBR grade II and in >14.2 majority of the participants (83.3%) were in MBR grade III. The present study also showed that in ER PR STATUS was 40.0% TO 14.3% for the negative patients and no significance in the Her2neu status.

Conclusion

This study led to the conclusion that NLR, PLR & RDW even though easily available test from a haemogram, was very productive in analyzing breast cancer and its relation to different stages of breast cancer ,and based on pathological grading we could be vigilant before going to the definitive treatment on Ca breast . The study demonstrated that higher the value of NLR, PLR, RDW there should be more evaluation to look for metastasis and disease progression. My study Included 100 patients majority are in the age group 50-60. The Cut off value for NLR was placed as </=3, and majority of the patients with high MBR & tumor grade comes (69.2 %) of grade 3 showed high NLR (>3).There was no change in NLR ratio with type of tumor (ductal or lobular) & menopause. This study showed a significant result (97.4 % vs 68.9%) for invasion of the tumor and it had a high NLR ratio. For patients with ER negative PR negative hormone status NLR was high showing bad prognosis.
PLR showed a significant difference ($p<0.001$) in </=200 and >200 between MBR grade I, II, &III. In </=200 group majority of the participants (50%) were in MBR grade II and in >200 all of the participants (100%) were in MBR grade III which was statistically significant. There was no association with invasion of the tumor with PLR (p value 0.012). ER negative, PR negative hormone status patients had significant high PLR.
For RDW, there is a significant difference ($p<0.001$) in </=14.2 and >14.2 between MBR grade I, II, &III. In </=14.2 group majority of the participants (51.4%) were in MBR grade II and in >14.2 majority of the participants (83.3%) were in MBR grade III. The post NACT patients showed that both NLR and PLR is significantly higher concluding that disease progression was associated with elevated NLR and PLR value.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

Bibilography

1. Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016 a systematic analysis for the global burden of disease study global burden o. JAMA Oncol. 2018;4(11):1553–68.
2. icmr. bd0f9984b48235a1c28a23c83713e039ae476321 @ cancerindia.org.in [Internet]. india: icmr; 2021. p. 1. Available from: http://cancerindia.org.in/cancer-statistics/
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Vol. 136, International Journal of Cancer. 2015. p. E359–86.
4. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391(10125):1023–75.
5. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018 Mar 17;391(10125):1023–75.
6. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.
7. Dhillon PK, Mathur P, Nandakumar A, Fitzmaurice C, Kumar GA, Mehrotra R, et al. The burden of cancers and their variations across the states of India: the Global Burden of Disease Study 1990–2016. Lancet Oncol. 2018;19(10):1289–306.
8. Masood S. Prognostic/predictive factors in breast cancer. Clin Lab Med. 2005 Dec;25(4):809-25 viii. doi: 10. 1016/j. cll. 2005. 08. 012. P 16308094. No Title.
9. Fitzgibbons PL, Page DL, Weaver D, Thor AD, Craig Allred D, Clark GM, et al. Prognostic Factors in Breast Cancer-Fitzgibbons et al. Arch Pathol Lab Med. 2000;124.
10. Grann VR, Troxel AB, Zojwalla NJ, Jacobson JS, Hershman D, Neugut AI. Hormone Receptor Status and Survival in a Population-Based Cohort of Patients with Breast Carcinoma. 2005; Available from: www.interscience.wiley.com
11. Alessandra Mancino, Toby Lawrence.NF-κB and tumor-associated macrophages Clin Cancer Res.2010 Feb 1; 16(3): 784–789. Published online 2010 Jan 26. doi: 10.1158/1078-0432.CCR-09-1015
12. Crumley A, Mcmillan DC, Mckernan M, Going JJ, Shearer CJ, Stuart RC. An elevated C-reactive protein concentration, prior to surgery, predicts poor cancer-specific survival in patients undergoing resection for gastro-oesophageal cancer. Br J Cancer [Internet]. 2006;94:1568–71. Available from: www.cancerresearchuk.org
13. Forrest LM, Mcmillan DC, Mcardle CS, Angerson WJ, Dunlop DJ. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. Br J Cancer [Internet]. 2003;89:1028–30. Available from: www.bjcancer.com
14. Sadik CD, Kim ND, Luster AD. Neutrophils cascading their way to inflammation. Vol. 32, Trends in Immunology. 2011. p. 452–60.
15. Miskolci V, Rollins J, Hai YV, Ghosh CC, Davidson D, Vancurova I. NFκB is persistently activated in continuously stimulated human neutrophils. Mol Med. 2007 Mar;13(3–4):134–42.
16. Son C-G, Shin J-W, Cho J-H, Cho C-K, Yun C-H, Han S-H. Induction of murine interleukin-1 beta expression by water-soluble com-ponents from Hericium erinaceum 1.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

17. Leitch EF, Chakrabarti M, Crozier JEM, McKee RF, Anderson JH, Horgan PG, et al. Comparison of the prognostic value of selected markers of the systemic inflammatory response in patients with colorectal cancer. Br J Cancer. 2007;97(9):1266–70.
18. Vano Y-A, Phane Oudard S, By M-A, Têtu P, Thibault C, Aboudagga H, et al. Optimal cut-off for neutrophil-to-lymphocyte ratio: Fact or Fantasy? A prospective cohort study in metastatic cancer patients. 2018; Available from: https://doi.org/10.1371/journal.pone.0195042
19. Proctor MJ, Mcmillan DC, Morrison DS, Fletcher CD, Horgan PG, Clarke SJ. A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. Br J Cancer [Internet]. 2012;107:695–9. Available from: www.bjcancer.com
20. Fö Z, Cz R, Gombos T, Borgulya G, Pozsonyi Z, Prohászka Z, et al. Red cell distribution width: a powerful prognostic marker in heart failure.
21. Riedl J, Posch F, Kö Nigsbrü Gge O, Lö Tsch F, Reitter E-M, Eigenbauer E, et al. Red Cell Distribution Width and Other Red Blood Cell Parameters in Patients with Cancer: Association with Risk of Venous Thromboembolism and Mortality. Available from: http://www.oenb.at/en/About-Us/Research-Promotion/The-OeNB-Anniversary-Fund.html
22. Wu L, Zou S, Wang C, Tan X, Yu M. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio in Chinese Han population from Chaoshan region in South China. BMC Cardiovasc Disord. 2019;19(1):1–5.
23. Azab B, Bhatt VR, Phookan J, Murukutla S, Kohn N, Terjanian T, et al. Usefulness of the Neutrophil-to-Lymphocyte Ratio in Predicting Short-and Long-Term Mortality in Breast Cancer Patients. Oncol. 2012;19:217–24.
24. Adinolfi E, Adinolfi E. New intriguing roles of ATP and its receptors in promoting tumor metastasis Presented by Maria P. Abbracchio. Purinergic Signal. 2013;9:487–90.
25. Ariad S, Seymour L, Bezwoda WR. Platelet-derived growth factor (PDGF) in plasma of breast cancer patients: Correlation with stage and rate of progression. Vol. 20, Breast Cancer Research and Treatment. 1991.
26. Goubran HA, Burnouf T, Radosevic M, El-Ekiaby M. The platelet-cancer loop. Eur J Intern Med [Internet]. 2013;24(5):393–400. Available from: http://dx.doi.org/10.1016/j.ejim.2013.01.017
27. Smyth MJ, Dunn GP, Schreiber RD. Cancer Immunosurveillance and Immunoediting: The Roles of Immunity in Suppressing Tumor Development and Shaping Tumor Immunogenicity. Adv Immunol. 2006;90(06):1–50.
28. Zhao Q-T, Yuan Z, Zhang H, Zhang X-P, Wang H-E, Wang Z-K, et al. Prognostic role of platelet to lymphocyte ratio in non-small cell lung cancers: A meta-analysis including 3,720 patients.
29. Tan D, Fu Y, Su Q, Wang H. Prognostic role of platelet–lymphocyte ratio in colorectal cancer. Medicine (Baltimore). 2016;95(24):e3837.
30. Zhang X, Zhao W, Yu Y, Qi X, Song L, Zhang C, et al. Clinicopathological and prognostic significance of platelet-lymphocyte ratio (PLR) in gastric cancer: an updated meta-analysis. Available from: https://doi.org/10.1186/s12957-020-01952-2
31. Templeton AJ, Ace O, ead McNamara MG, Al-Mubarak M, Vera-Badillo FE, Hermanns T, et al. Prognostic Role of Platelet to Lymphocyte Ratio in Solid Tumors: A Systematic Review and Meta-Analysis. 2014; Available from: http://cebp.aacrjournals.org/
32. Huang D-P, Ma R-M, Xiang Y-Q. Utility of Red Cell Distribution Width as a Prognostic Factor in Young Breast Cancer Patients. Available from: www.md-journal.com
33. Warwick R, Mediratta N, Shackcloth M, Shaw M, Mcshane J, Poullis M. Preoperative red cell distribution width in patients undergoing pulmonary resections for non-small-cell lung cancer. 2013; Available from:

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

https://academic.oup.com/ejcts/article/45/1/108/567289
34. Albayrak S, Zengin K, Tanik S, Bakirtas H, Imamoglu A, Gurdal M. Red cell distribution width as a predictor of prostate cancer progression. Asian Pacific J Cancer Prev. 2014;15(18):7781–4.
35. Kust D, Lucijanic M, Urch K, Samija I, Celap I, Kruljac I, et al. Clinical and prognostic significance of anisocytosis measured as a red cell distribution width in patients with colorectal cancer. An Int J Med [Internet]. 2017;361–7. Available from: https://academic.oup.com/qjmed/article/110/6/361/2875722
36. Pinar Yarici, Uygar Demir, Emre Bozkurt, Gurhan R Isil, et al The role of red cell distribution width in the prognosis of patients with gastric cancer October 2016 Cancer biomarkers, section A of disease markers 18(1):1-7
37. Giralt J, Stoeckli SJ, St Gallen K, Xavier León S, Zhou L, Hsueh C-Y, et al. Pretreatment Level of Red Cell Distribution Width as a Prognostic Indicator for Survival in a Large Cohort Study of Male Laryngeal Squamous Carcinoma. Front Oncol | www.frontiersin.org [Internet]. 2019;1:271. Available from: www.frontiersin.org
38. Yao D, Wang Z, Cai H, Li Y, Li B. Relationship between red cell distribution width and prognosis in patients with breast cancer after operation: a retrospective cohort study. Biosci Rep [Internet]. 2019;20190740. Available from: https://doi.org/10.1042/BSR20190740
39. Ren K, Yin Y, Shao Y, Wang S. Cancer Management and Research Dovepress Prognostic role of derived neutrophil-to-lymphocyte ratio in surgical triple-negative breast cancer. Cancer Manag Res [Internet]. 2018;10–4891. Available from: http://dx.doi.org/10.2147/CMAR.S180695
40. Hu JJ, Urbanic JJ, Case LD, Takita C, Wright JL, Brown DR, et al. JOURNAL OF CLINICAL ONCOLOGY Association Between Inflammatory Biomarker C-Reactive Protein and Radiotherapy-Induced Early Adverse Skin Reactions in a Multiracial/Ethnic Breast Cancer Population. J Clin Oncol [Internet]. 2018;36:2473–82. Available from: https://doi.org/10.1200/JCO.2017.
41. Wan J, Luo P, Du X, Yan H. Preoperative red cell distribution width predicts postoperative cognitive dysfunction after coronary artery bypass grafting. Biosci Rep [Internet]. 2020; Available from: https://doi.org/10.1042/BSR20194448