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Exploring the neutrophil-to-lymphocyte ratio as a prognostic biomarker in triple-negative breast cancer

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Abstract

Triple-negative breast cancer is a subtype characterized by the absence of estrogen receptor, progesterone Receptor, and Human Epidermal Growth Factor Receptor 2 receptors, limiting treatment options primarily to chemotherapy due to lack of targeted therapies typically used for other breast cancer types, hence necessitating research for improved therapeutic strategies and outcomes. The neutrophil and lymphocyte percentages, absolute counts, and the ratio of neutrophils to lymphocytes were evaluated in peripheral blood of 81 patients with triple-negative breast cancer (TNBC) and 25 healthy controls. This study observed trend of high neutrophil percentage was observed in patients with positive lymph node status as compared to negative lymph node status. Significant high absolute neutrophil count was observed in patients with positive LN status, High BR score and presence of metastasis. A trend of high neutrophil to lymphocyte ratio was observed in patients with presence of perineural invasion, presence of necrosis, and patients with presence of metastasis.

Keywords: TNBC; NLR; DFS; OS

1. Introduction

TNBC are breast cancer type which denoted by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) amplification. Consequently, this molecular profile limits the response of TNBC to common hormonally active treatment (including receptors targeting biologicals like trastuzumab) and pathological perturbations widely considered as a target of this treatment. So, it comes as no surprise that this entity of the disease has remained an enigma to scientists. TNBC is often known for being more aggressive and metastatic; a higher rate of relapse and an early occurrence as often observed in women mostly under the age of 35, all of this in the absence of the estrogen and progesterone receptors. In recent years, there has been a noticeable effort in recognizing those specific biomarkers that may accurately guide treatment selection, and predict survival outcomes for patients with TNBC. An NLR approaching the critical threshold may result in many markers of host disease being elevated which can lead to adverse health outcomes and high short-term mortality. NLR, which is the ratio of absolute neutrophil count to absolute lymphocyte count, reflects the balance between the systemic inflammatory response and the host immune response. In several cancer cases, there is an association between high-level NLR and the worsening of the prognosis and the tumors become more malignant, including breast cancer. NLR in TNBC is a subject matter being actively studied not only for its functional significance but for the potential implications it presents.

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2. Material and methods

The neutrophil and lymphocyte percentages, absolute counts, and the ratio of neutrophils to lymphocytes were evaluated in peripheral blood of 81 patients with triple-negative breast cancer (TNBC) and 25 healthy controls. Detailed clinical and pathological history of the patients including age, menopausal status, tumor size, lymph node status, American Joint Committee on Cancer (AJCC) TNM stage, histopathological status, tumor grade, Bloom-Richardson (BR) score, perinodal extension, perineural invasion, necrosis, disease status and treatment offered was retrieved from the records maintained by Medical Record Department of the institute and was documented in the laboratory registers. Informed consent forms of all the patients enrolled in this study were obtained. This study was approved by Scientific Review and Ethics committees of the institute.

Table 1 Clinical and Pathological characteristics of the patients

Characteristics		**N**	**(%)**
Age (Median age: 47 years)	≤47	50	50
	>47	50	50
Menopausal status	Premenopausal	46	46
	Postmenopausal	47	47
	Perimenopausal	07	07
Tumor Size	T1	08	08
	T2	77	77
	T3	11	11
	T4	04	04
Lymph node status	Positive	43	43
	Negative	57	57
Stage	I	02	02
	II	75	75
	III	23	23
	IV	00	00
Histological Type	IDC	81	81
	IDC + DCIS	17	17
	IDC + Medullary	02	02
Histological Grade	I	01	01
	II	26	26
	III	66	66
	Unknown	07	07
BR Score	Low (3-5)	02	02
	Intermediate (6-7)	27	27
	High (8-9)	62	62
	Unknown	09	09
Perinodal extension	Present	21	21
	Absent	79	79

Perineural invasion	Present	06	06
	Absent	94	94
Necrosis	Present	42	42
	Absent	58	58
Metastasis	Metastasis	15	15
	Remission	85	85
Disease status	Dead	15	15
	Alive	85	85

3. Results

3.1. Healthy Controls

In peripheral blood of healthy Controls, Neutrophils were ranged between 48.3% to 77.5% with a mean value of 57.7±7.05%, Lymphocytes was ranged between 13.6 to 39.1% with a mean value of 30.3±6.8, Absolute Neutrophils Count (ANC) was ranged between 2 to 8.3 ($x10^3/\mu L$) with a mean value of 4.4±1.47, Absolute Lymphocytes Count (ALC) was ranged between 1.4 to 3.3 ($x10^3/\mu L$) with a mean value of 2.2±0.58 and Neutrophil to Lymphocyte Ratio (NLR) was in the range of 1.2 to 5.5 with a mean value of 2.1±0.96 (Table 2).

Table 2 Neutrophils and Lymphocytes percentage and their count ratio in Healthy Controls

	Range	**Mean±S.D.**
Neutrophils	48.3-77.5(%)	57.7±7.05
Lymphocytes	13.6-39.1(%)	30.3±6.8
ANC	2-8.3($x10^3/\mu L$)	4.4±1.47
ALC	1.4-3.3($x10^3/\mu L$)	2.2±0.58
NLR	1.2-5.5	2.1±0.96

3.2. Triple Negative Breast Cancer Patients (TNBC)

Out of 100 TNBC patients, pre-operative data regarding differential WBC count was available of 81 TNBC patients. In TNBC patients, Neutrophils were ranged between 47.1-70.27(%) with a mean value of 64.34 ± 8.96, lymphocytes were ranged between 16.18-41.1 % with a mean value of 27.94± 6.32, Absolute Neutrophil Count (ANC) was ranged between 1.4-7.8 ($x10^3/\mu L$) with a mean value of 5.10 ± 1.70, Absolute Lymphocyte Count (ALC) was ranged between 0.7-4.9 ($x10^3/\mu L$) with a mean value of 2.17 ± 0.70 and Neutrophil to Lymphocyte Ratio (NLR) was ranged between of 1.14-4.35 with a mean value of 2.44 ± 0.88 (Table 3).

Table 3 Neutrophils and Lymphocytes percentage and their count ratio in TNBC patients

	Range	**Mean±S.D.**
Neutrophils	47.1-70.27(%)	64.34 ± 8.96
Lymphocytes	16.18-41.1 (%)	27.94± 6.32
ANC	1.4-7.8 ($x10^3/\mu L$)	5.10 ± 1.70
ALC	0.7-4.9 ($x10^3/\mu L$)	2.17 ± 0.70
NLR	1.14-4.35	2.44 ± 0.88

3.3. Comparison of Neutrophils and Lymphocytes percentage and their percentage count ratio of TNBC patients with Healthy Controls

In comparison with healthy controls, significant higher mean percentage value of Neutrophils was observed in TNBC patients (57.7±7.05 vs 64.34 ± 8.96, p=0.003), Also in comparison to healthy controls, significant low mean percentage of Lymphocyte was also observed in TNBC patients (30.3±6.8 vs 27.94± 6.32, p=0.001), further ANC (4.4±1.47 vs 5.10 ± 1.70, p=0.05) and NLR (1.2-5.5 vs 2.44 ± 0.88, p=0.04) was observed significantly higher in TNBC patients as compared to healthy controls, while there is no significant difference was noted in ALC (1.4-3.3vs 2.17 ± 0.70) between healthy controls and TNBC patients (Table 4).

Table 4 Comparison of Neutrophils and Lymphocytes percentage count and their Ratio of TNBC patients with Healthy Controls

		Mean± S.D.	**p value**
Neutrophils	HC	57.7±7.05	0.003
	TNBC	64.34 ± 8.96	
Lymphocytes	HC	30.3±6.8	0.001
	TNBC	27.94± 6.32	
ANC	HC	4.4±1.47	0.05
	TNBC	5.10 ± 1.70	
ALC	HC	1.4-3.3	0.63
	TNBC	2.17 ± 0.70	
NLR	HC	1.2-5.5	0.04
	TNBC	2.44 ± 0.88	

3.4. Correlation of Neutrophils and Absolute Neutrophils Count (ANC) with Clinicopathological Parameters

As table 5 indicates, regarding clinicopathological parameters, an increased mean value of neutrophils and ANC was observed in patients with age ≤48 years as compared to >48 of age, patients with peri menopausal status patients with smaller tumor size showed an increased mean value of neutrophils and ANC in peripheral blood as compared to their respective counterparts. Further patients with lymph node positive status reported a trend of increased mean value of neutrophils (p=0.07) and significant higher ANC in peripheral blood as compared to negative lymph node status (p=0.05). Moreover, it is observed that patients with early disease stage showed an increased mean value of neutrophils and ANC in peripheral blood. When patients sub grouped according to histological type, patients with IDC subtype showed an increased mean value of neutrophils while patients with IDC+DCIS subtype showed increased ANC in peripheral blood. According to histological grade, patients with grade III tumors showed an increased mean value of neutrophils and ANC in peripheral blood as compared to grade I and grade II tumors. In the subgroup of BR score, patients with high BR score showed increased mean value of neutrophils and trend of high ANC in peripheral blood (p=0.07). It was also observed that patient with presence of perinodal extension showed an increased mean value of neutrophils and absolute neutrophils count in peripheral blood. Further it has been observed that patients with necrotic tumors showed an increased mean value of neutrophils and ANC in peripheral blood. In relation to metastasis, an increased mean value of neutrophils and a trend of high ANC was observed in peripheral blood of patients who developed metastasis.

Table 5 Correlation of Neutrophils and Absolute Neutrophils Count (ANC) with Clinicopathological Parameters

characteristics		**N**	**Neutrophils Mean ± SD**	**F Value**	**P Value**	**ANC Mean ± SD**	**F Value**	**P Value**
Age	≤48	43	53 ± 7.05	0.60	0.43	4.12 ± 1.14	0.08	0.92
	>48	38	44 ± 8.32			4.10 ± 1.49		
Menopausal status	Pre	37	54 ± 6.90	0.51	0.60	4.31 ± 1.50	0.06	0.93
	Post	37	43 ± 7.96			3.90 ± 1.49		
	Peri	07	57 ± 6.43			4.42 ± 1.53		
Tumor size	T1+ T2	61	52 ± 6.98	0.92	0.34	5.10 ± 2.50	2.47	0.12
	T3+ T4	20	40 ± 7.54			4.90 ± 1.45		
Lymph node status	Positive	45	53 ± 6.80	2.62	0.07	4.50 ± 2.51	3.30	0.05
	Negative	36	40 ± 5.70			3.00 ± 1.51		
Disease Stage	I	02	50 ± 4.98	0.48	0.63	4.60 ± 1.00	2.19	0.11
	II	59	52 ± 5.58			4.80 ± 1.50		
	III	20	40 ± 4.80			2.60 ± 1.45		
Histopathological type	IDC	66	50 ± 5.00	0.62	0.53	4.90 ± 2.12	0.55	0.57
	IDC+DCIS	14	42 ± 4.34			5.0. ± 1.00		
	IDC+Medullary	01	45 ± 4.53			4.80 ± 2.30		
Histopathological grade	I	01	45 ± 4.47	0.80	0.44	3.5 ± 1.45	0.96	0.38
	II	23	43 ± 4.50			3.43 ± 2.70		
	III	52	53 ± 4.50			4.60 ± 1.50		
BR Score	Low	02	50 ± 5.70	1.19	0.10	3.30 ± 1.80	2.75	0.07
	Intermediate	21	42 ± 4.50			4.10 ± 4.20		
	High	49	51 ± 5.50			5.20 ± 1.42		
Perinodal extension	Present	16	56 ± 5.51	0.36	0.54	5.48 ± 2.00	0.54	0.46
	Absent	65	47 ± 5.50			3.90 ± 2.10		
Perineural invasion	Present	05	56 ± 5.43	0.23	0.62	4.90 ± 3.00	0.07	0.93
	Absent	76	48 ± 4.30			4.13 ± 1.83		
Necrosis	Present	33	54 ± 6.01	0.58	0.44	5.12 ± 3.00	0.12	0.72
	Absent	48	45 ± 5.80			4.20± 1.32		
Metastasis	Absent	70	39 ± 4.54	1.12	0.09	4.00 ± 1.50	2.95	0.08
	Present	11	51 ± 4.70			5.87 ± 2.50		

3.5. Correlation of Lymphocytes and Absolute Lymphocytes Count (ALC) with Clinicopathological Parameters

As table 6 indicates, regarding clinicopathological parameters, an increased mean value of lymphocytes and ALC was observed in patients with age ≤48 years patients with peri menopausal patients, patients with smaller tumor size showed an increased mean value of lymphocytes and ALC in peripheral blood as compared to their respective counterparts. Further patients with lymph node positive and negative status reported no difference in mean value of lymphocytes while increased ALC in peripheral blood in patients with lymph node negative status. Moreover, it is observed that patients with early disease stage and advance disease stage showed no difference in mean value of lymphocytes and ALC in peripheral blood. When patients sub grouped according to histological type, patients with IDC

subtype showed a decreased mean value of ALC in peripheral blood as compared to other subtypes. According to histological grade, patients with grade I tumors showed an increased mean value of lymphocytes and ALC in peripheral blood as compared to grade I and grade II tumors. In the subgroup of BR score, patients with high BR score showed increased mean value of lymphocytes and ALC in peripheral blood. It was also observed that patient with absence of perinodal extension showed an increased mean value of lymphocytes and ALC in peripheral blood. Further it has been observed that patients with absence of necrosis showed an increased mean value of lymphocytes and ALC in peripheral blood. In relation to metastasis, an increased mean value of lymphocytes (p=0.07) and a trend of high ALC (p=0.08) was observed in peripheral blood of patients with absence of metastasis.

Table 6 Correlation of Lymphocytes and Absolute Lymphocytes Count (ALC) with Clinicopathological Parameters

characteristics		**N**	**Lymphocytes Mean ± SD**	**F Value**	**P Value**	**ALC Mean ± SD**	**F Value**	**P Value**
Age	≤48	43	14.46 ± 6.50	0.30	0.58	1.48 ± 0.50	0.17	0.67
	>48	38	12.52 ± 6.50			1.44 ± 0.50		
Menopausal status	Pre	37	10.45 ± 4.50	0.30	0.73	1.48 ± 0.50	0.29	0.74
	Post	37	11.54 ± 5.00			1.42 ± 0.50		
	Peri	07	11.42 ± 4.10			1.57 ± 0.53		
Tumor size	T1+ T2	61	14.45 ± 3.48	1.90	0.17	1.46 ± 0.50	0.03	0.95
	T3+ T4	20	13.63 ± 3.49			1.47 ± 0.51		
Lymph node status	Positive	45	15.46 ± 3.50	0.29	0.58	1.43 ± 0.50	0.48	0.48
	Negative	36	15.52 ± 3.21			1.51 ± 0.50		
Disease Stage	I	02	14.50 ± 3.29	0.94	0.39	1.50 ± 0.70	0.06	0.99
	II	59	14.44 ± 3.80			1.46 ± 0.50		
	III	20	14.63 ± 4.00			1.47 ± 0.51		
Histopathological type	IDC	66	12.48 ± 3.50	0.65	0.52	1.45 ± 0.50	0.75	0.47
	IDC+DCIS	14	13.57 ± 3.51			1.57 ± 0.51		
	IDC+Medullary	01	13.69 ± 3.44			1.59 ± 0.63		
Histopathological grade	I	01	14.00 ± 4.12	1.96	0.14	2.15 ± 0.80	0.72	0.48
	II	23	13.36 ± 3.98			1.41 ± 0.50		
	III	52	13.12 ± 3.12			1.51 ± 0.50		
BR Score	Low	02	13.00 ± 2.00	2.15	0.12	1.50 ± 0.70	0.711	0.49
	Intermediate	21	12.61 ± 3.49			1.40 ± 0.50		
	High	49	13.42 ± 2.90			1.56 ± 0.50		
Perinodal extension	Present	16	13.56 ± 4.00	0.37	0.54	1.43 ± 0.51	0.07	0.78
	Absent	65	14.47 ± 3.50			1.47 ± 0.50		
Perineural invasion	Present	05	13.60 ± 3.54	0.23	0.62	1.60 ± 0.54	0.36	0.54
	Absent	76	12.48 ± 3.50			1.45 ± 0.50		
Necrosis	Present	33	14.12 ± 4.50	0.13	0.71	1.40 ± 0.50	0.04	0.83
	Absent	48	14.51 ± 3.90			1.47 ± 0.50		
Metastasis	Absent	70	14.89 ± 4.56	1.94	0.07	2.53 ± 0.50	1.96	0.08
	Present	11	12.30 ± 2.32			1.27 ± 0.46		

3.6. Correlation of Neutrophil to lymphocyte ratio (NLR) with Clinicopathological Parameters

As table 7 depicts, in relation to clinicopathological variables, an increased mean value of NLR was observed in patients with age ≤48 years, patients with pre-menopausal patients, patients with smaller tumor size, patients with lymph node positive status and patients with advance disease stage showed increased mean value of NLR in peripheral blood as compared to their respective counterparts. When patients sub grouped according to histological type, patients with IDC+ Medullary subtype showed an increased mean value of NLR in peripheral blood as compared to other subtypes. According to histological grade, patients with grade III tumors showed an increased mean value of NLR in peripheral blood as compared to grade I and grade II tumors. In the subgroup of BR score, there was no difference observed in NLR of patients with high, intermediate and low BR score. It was also observed that patient with presence of perinodal extension showed slight increased mean value of NLR in peripheral blood. Also, a trend of increased mean value of NLR was observed in patients with presence of perineural invasion (p=0.07). Further it is noted that patients with presence of necrosis showed trend of increased mean value of NLR in peripheral blood (p=0.08). In relation to metastasis, trend of increased mean value of NLR was observed in peripheral blood of patients with presence of metastasis (p=0.07).

Table 7 Correlation of Neutrophil to lymphocyte ratio (NLR) with Clinicopathological Parameters

characteristics		**N**	**NLR Mean ± SD**	**F Value**	**P Value**
Age	≤48	43	4.46 ± 2.50	0.30	0.58
	>48	38	3.52 ± 2.42		
Menopausal status	Pre	37	4.45 ± 2.50	0.30	0.73
	Post	37	3.54 ± 2.00		
	Peri	07	3.42 ± 1.10		
Tumor size	T1+ T2	61	4.45 ± 2.48	1.90	0.17
	T3+ T4	20	3.63 ± 1.49		
Lymph node status	Positive	45	5.46 ± 2.50	0.29	0.58
	Negative	36	4.52 ± 1.21		
Disease Stage	I	02	3.50 ± 1.29	0.94	0.39
	II	59	4.44 ± 2.80		
	III	20	4.63 ± 2.00		
Histopathological type	IDC	66	3.48 ± 1.50	0.65	0.52
	IDC+DCIS	14	3.57 ± 1.51		
	IDC+Medullary	01	3.69 ± 1.44		
Histopathological grade	I	01	4.00 ± 2.12	1.96	0.14
	II	23	4.36 ± 1.98		
	III	52	4.69 ± 2.12		
BR Score	Low	02	4.00 ± 1.62	2.15	0.12
	Intermediate	21	4.61 ± 1.49		
	High	49	4.42 ± 2.00		
Perinodal extension	Present	16	4.56 ± 2.10	0.37	0.54
	Absent	65	4.47 ± 2.50		
Perineural invasion	Present	05	5.60 ± 2.54	1.23	0.07
	Absent	76	4.48 ± 2.50		
Necrosis	Present	33	5.12 ± 2.49	1.13	0.08

	Absent	48	4.51 ± 2.90		
Metastasis	Absent	70	2.30 ± 1.32	1.94	0.07
	Present	11	4.89 ± 2.56		

3.7. Survival analysis of neutrophil percentage and absolute neutrophil count in peripheral blood

The disease free and overall survival analysis of percentage of neutrophils was evaluated using Kaplan and Meier univariate survival analysis. The mean follow-up time was 40.05± 1.50 months with maximum follow-up time 72 months. With respect to DFS, revealed a higher incidence of disease relapse in patients with low percentage of neutrophils (17%, 07/41, 62.50 ± 4.25) as compared to patients with high percentage of neutrophils in peripheral blood (10%, 04/40, 67.23 ± 2.83, χ^2= 0.94, df= 1, p=0.33. With respect to overall survival, univariate survival analysis for OS revealed a significant higher incidence of death in patients with low percentage of neutrophils (15%, 07/41, 61.72 ± 4.15) as compared patients with high percentage of neutrophils in peripheral blood (04%, 04/40, 64.00 ± 2.77, df= 1, p=0.33).

Similarly, with respect to DFS, revealed a higher incidence of disease relapse in patients with low absolute neutrophil count (20%, 09/46, 60.95 ± 4.02) as compared to patients with high absolute neutrophil count in peripheral blood (06%, 02/33, 59.04 ± 2.02, χ^2= 2.70, df= 1, p=0.10), With respect to overall survival, univariate survival analysis for OS revealed a significant higher incidence of death in patients with low absolute neutrophil count (20%, 09/46, 61.13 ± 3.71) as compared patients with high absolute neutrophil count in peripheral blood (06%, 02/33, 59.22 ± 1.87, df= 1, p=0.11), (Table 8).

Table 8 Survival analysis of neutrophil percentage and absolute neutrophil count in peripheral blood

Percentage of Neutrophils	**N**	**DFS in months Mean ± SE**	**Remission N (%)**	**Relapsed N (%)**
Low	41	62.50 ± 4.25	34 (83)	07 (17)
High	40	67.23 ± 2.83	36 (90)	04 (10)
			χ^2= 0.94, df= 1, p=0.33	
Percentage of Neutrophils	N	OS in months Mean ± SE	Alive N (%)	Dead N (%)
Low	41	61.72 ± 4.15	34 (83)	07 (15)
High	40	64.00 ± 2.77	36 (90)	04 (04)
			χ^2= 0.93, df= 1, p=0.33	
Absolute neutrophil count	N	DFS in months Mean ± SE	Remission N (%)	Relapsed N (%)
Low	46	60.95 ± 4.02	37 (80)	09 (20)
High	33	59.04 ± 2.02	31 (94)	02 (06)
			χ^2= 2.70, df= 1, p=0.10	
Absolute neutrophil count	N	OS in months Mean ± SE	Alive N (%)	Dead N (%)
Low	46	61.13 ± 3.71	37 (80)	09 (20)
High	33	59.22 ± 1.87	31 (94)	02 (06)
			χ^2= 2.52, df= 1, p=0.11	

3.8. Survival analysis of lymphocyte percentage and absolute lymphocyte count in peripheral blood

The disease free and overall survival analysis of percentage of lymphocytes was evaluated using Kaplan and Meier univariate survival analysis. The mean follow-up time was 40.05± 1.50 months with maximum follow-up time 72 months. With respect to DFS, revealed a higher incidence of disease relapse in patients with high percentage of lymphocytes (18%, 07/39, 62.34 ± 4.24) as compared to patients with low percentage of lymphocytes in peripheral blood (07%, 03/40, 63.63 ± 2.39, χ^2= 1.86, df= 1, p=0.17. With respect to overall survival, univariate survival analysis for OS revealed a significant higher incidence of death in patients with high percentage of lymphocytes (18%, 07/39,

61.87 ± 4.10) as compared patients with low percentage of lymphocytes in peripheral blood (04%, 04/40, 61.87 ± 4.10, df= 1, p=0.18).

With respect to DFS, revealed a higher incidence of disease relapse in patients with low absolute lymphocyte count (19%, 08/42, 57.81 ± 3.79) as compared to patients with high absolute lymphocyte count in peripheral blood (08%, 03/37, 68.59 ± 3.42, χ^2= 2.34, df= 1, p=0.12), With respect to overall survival, univariate survival analysis for OS revealed a significant higher incidence of death in patients with low absolute lymphocyte count (19%, 08/42, 57.99 ± 3.53) as compared patients with high absolute lymphocyte count in peripheral blood (08%, 03/37, 68.17 ± 3.44, df= 1, p=0.10), (Table 9).

Table 9 Survival analysis of lymphocyte percentage and absolute lymphocyte count in peripheral blood

Percentage of Lymphocytes	**N**	**DFS in months Mean ± SE**	**Remission N (%)**	**Relapsed N (%)**
Low	40	63.63 ± 2.39	37 (93)	03 (07)
High	39	62.34 ± 4.24	32 (82)	07 (18)
			χ^2= 1.86, df= 1, p=0.17	
Percentage of Lymphocytes	N	OS in months Mean ± SE	Alive N (%)	Dead N (%)
Low	40	63.63 ± 2.36	37 (93)	03 (07)
High	39	61.87 ± 4.10	32 (82)	07 (18)
			χ^2= 1.78, df= 1, p=0.18	
Absolute lymphocyte count	N	DFS in months Mean ± SE	Remission N (%)	Relapsed N (%)
Low	42	57.81 ± 3.79	34 (81)	08 (19)
High	37	68.59 ± 3.42	34 (92)	03 (08)
			χ^2= 2.34, df= 1, p=0.12	
Absolute lymphocyte count	N	OS in months Mean ± SE	Alive N (%)	Dead N (%)
Low	42	57.99 ± 3.53	34 (81)	08 (19)
High	37	68.17 ± 3.44	34 (92)	03 (08)
			χ^2= 2.60, df= 1, p=0.10	

3.9. Survival analysis of Neutrophil to lymphocyte ratio in peripheral blood

Table 10 Survival analysis of Neutrophil to lymphocyte ratio in peripheral blood

Neutrophil to lymphocyte ratio	**N**	**DFS in months Mean ± SE**	**Remission N (%)**	**Relapsed N (%)**
Low	40	62.71 ± 4.13	33 (83)	07 (17)
High	39	61.92 ± 2.81	35 (90)	04 (10)
			χ^2= 0.79, df= 1, p=0.37	
Neutrophil to lymphocyte ratio	N	OS in months Mean ± SE	Alive N (%)	Dead N (%)
Low	40	62.25 ± 4.00	33 (83)	07 (17)
High	39	62.07 ± 2.69	35 (90)	04 (10)
			χ^2= 0.70, df= 1, p=0.40	

With respect to DFS, revealed a higher incidence of disease relapse in patients with low neutrophil to lymphocyte ratio (17%, 07/40, 62.71 ± 4.13) as compared to patients with high neutrophil to lymphocyte ratio in peripheral blood (10%, 04/39, 61.92 ± 2.81, χ^2= 0.79, df= 1, p=0.37), With respect to overall survival, univariate survival analysis for OS revealed a significant higher incidence of death in patients with low neutrophil to lymphocyte ratio (17%, 07/40, 62.25 ± 4.00)

as compared patients with high neutrophil to lymphocyte ratio peripheral blood (10%, 04/39, 62.07 ± 2.69, df= 1, p=0.40), (Table 10).

4. Discussion

In the present study, significant high neutrophil count was observed in pretherapeutic peripheral blood of TNBC patients as compared to peripheral blood of healthy controls. A study on a TNBC reported the same supportive results (Zheng et al.,2023). Further, present study reported significant low lymphocyte count in peripheral blood of TNBC as compared to healthy controls. Similar results in TNBC were already reported (Afghahi et al.,2018). Further the current study observed significant high absolute neutrophil count in TNBC as compared to healthy controls. Consistent results of this findings were reported in patients with breast cancer (Yoon et al.,2010). However, there is no such difference was observed for absolute lymphocyte count in TNBC and healthy controls. Additionally, patients with TNBC showed high neutrophil to lymphocyte ratio in TNBC as compared to healthy controls. There are several studies reported high neutrophil to lymphocyte ratio in breast cancer and TNBC (Corbeau et al.,2020, Kim et al.,2021). In the present study no correlation was observed between neutrophil/ absolute neutrophil count and clinicopathological parameters other than lymph node status, BR score and disease metastasis. The study observed patients with positive lymph node status showed high neutrophil and absolute neutrophil count. A study on a head and neck cancer also found that patients with positive lymph node status showed higher absolute neutrophil count than those with negative lymph node status (Khan et al.,2023). Regarding the BR score, patients with high BR score showed high absolute neutrophil count. However, there is no data available showing relation between BR score and absolute neutrophil count. In relation to metastasis, patients with presence of metastasis showed high absolute neutrophil count. Again, there is no data available stating the relationship between absolute neutrophil count and metastasis.

Regarding neutrophil to lymphocyte ratio, it was observed that patients with presence of perineural invasion, necrosis and metastasis showed high neutrophil to lymphocyte ratio compared to their respective counter parts. Studies on colorectal cancer and squamous cell carcinoma showed patients with presence of perineural invasion and metastasis had significantly higher neutrophil to lymphocyte ratio compared to those without perineural invasion and absence of metastasis (Jakubowska et al.,2022, Khan et al.,2023). Survival analysis was also carried for the neutrophil percentage, absolute neutrophil count, absolute lymphocyte count and neutrophil to lymphocyte ratio in peripheral blood with clinicopathological characteristics. However, no significant results observed in present study.

5. Conclusion

A trend of high neutrophil percentage was observed in patients with positive lymph node status as compared to negative lymph node status. Significant high absolute neutrophil count was observed in patients with positive LN status, High BR score and presence of metastasis. A trend of high neutrophil to lymphocyte ratio was observed in patients with presence of perineural invasion, presence of necrosis, and patients with presence of metastasis. Hence, high NLR ratio associated with unfavorable histopathological parameters and disease metastasis and targeted to lower down the ratio of NLR.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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