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Prediction of prognosis in breast cancer patients based on neutrophil to lymphocyte ratio in a tertiary centre

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Abstract

In recent decade there has been a substantial increase in breast cancer both in developed and developing countries. It's also has been the major cause of mortality in women, despite much progress in treatment for breast cancer. There is always a debate in assessment of prognosis in breast cancer. Inflammation play a major role in pathogenesis of breast cancer based of the cell type.

Neutrophil-to- lymphocyte ratio is a simple parameter which helps in predicting the prognosis of the patient. In this study, we would like to analyse peripheral blood neutrophil-lymphocyte ratio (NLR) in breast cancer patients and its correlation with disease staging. This cross-sectional study was conducted in R.L Jalappa hospital. A total of 30 female patients with breast cancer met the inclusion criteria. Exclusion criteria included clinical evidence of active infection, presence of haematological disorders, acute as well as chronic inflammatory or autoimmune diseases, or prior steroid therapy.

There was no association between the tumour size and age of patients with NLR. There was a significant relationship between NLR and staging of the disease.

Keywords: Breast cancer, neutrophil, lymphocyte ratio, tertiary centre

Introduction

Worldwide, 2.1 million newly diagnosed female breast cancer cases in 2018, have been diagnosed, accounting for almost 1 in 4 cancer cases among women ^[1]. The disease is the most frequently diagnosed cancer in the vast majority of the countries and is also the leading cause of cancer death in over 100 countries ^[1].

India along with United States and China collectively accounts for almost one third of the global breast cancer burden ^[2]. Indian women having breast cancer are found a decade younger in comparison to western women suggesting that breast cancer occurs at a younger premenopausal age in India ^[2]. The personal and family history of breast cancer, age, overweight, menstrual history, genetics, radiation to chest or face before age 30, pregnancy/breast feeding, race/ethnicity, hormone replacement therapy, alcohol consumption, dense breast, lack of exercise, smoking are contributing factors of breast cancer ^[3].

Staging of breast cancer is used to determine the survival rate of patients, this approach mandates for more investigations to the patient and its time consuming.

It is extremely important to discover one kind of parameter that can reflect the origin and development of tumour, and even the prognosis of the patient.

Immune system plays a vital role in tumour genesis. Here we analyse neutrophil lymphocyte ration in breast and its co relation with tumour size, staging and prognosis.

Objectives

1. To evaluate the neutrophil- lymphocyte ratio.
2. To evaluate the of neutrophil-lymphocyte ratio in breast cancer and its correlation with disease staging.
3. To study the prognosis in terms of metastasis and response assessment.

Materials & Methods

1. Design of study-cross sectional study
2. Total number of study subjects: 30

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Mode of selection of subjects-This study will be conducted in the Department of General Surgery, R.L. Jalappa Hospital, Kolar

It's a cross sectional from July 2019 to 2020 all patients diagnosed with carcinoma breast. Statistical analysis was done using SPSS version 20 software. Student t-test and chi-square tests were used. The t-test was used to compare two sets of quantitative data. The level of 0.05 was considered as significant.

Results

Age distribution among subjects

Table 1: Age distribution among subjects

		Count	%
Age	<40 years	5	16.7%
	41 to 50 years	11	36.7%
	51 to 60 years	9	30.0%
	>60 years	5	16.7%
	Total	30	100.0%

In the study 16.7% were in the age group <40 years, 36.7% were in the age group 41 to 50 years, 30% were in the age group 51 to 60 years, 16.7% were in the age group >60 years.

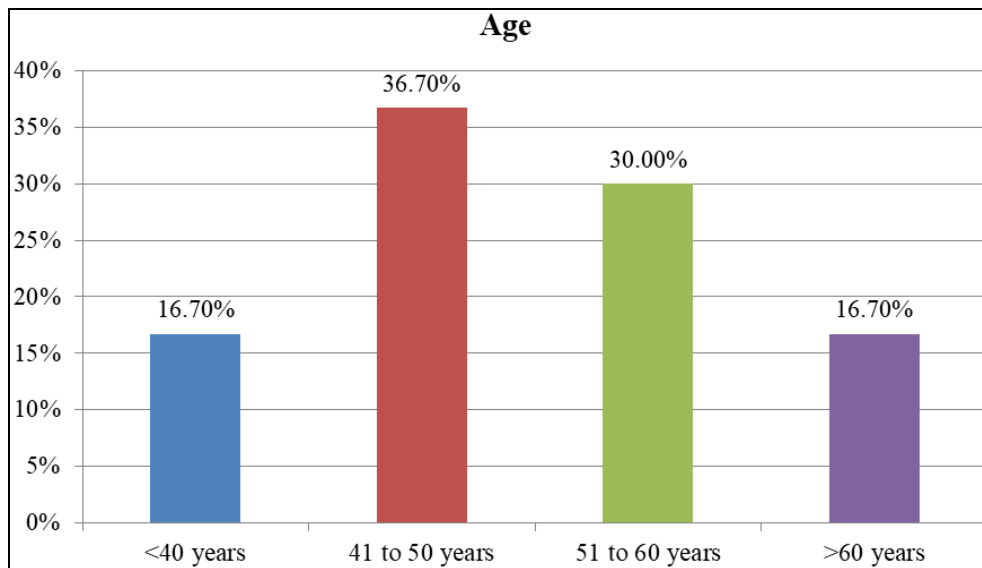


Fig 1: Bar diagram showing Age distribution among subjects

Table 2: Pre or Post Treatment distribution

		Count	%
PRE/POST	Post	26	86.7%
	Pre	4	13.3%

In the study 86.7% were pre and 13.3% were post treatment.

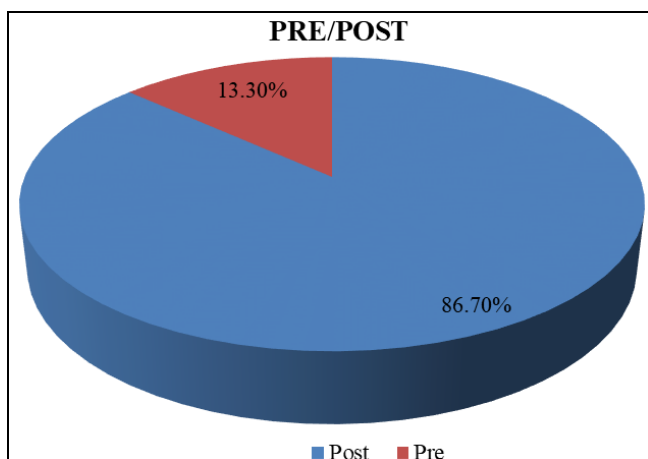


Fig 2: Pie diagram showing Pre or Post Treatment distribute

Table 3: Stage of Tumour distribution among subjects

		Count	%
Stage	II	16	53.3%
	III	11	36.7%
	IV	3	10.0%

In the study 53.3% were in stage II, 36.7% were in stage III and 10% were in stage IV.

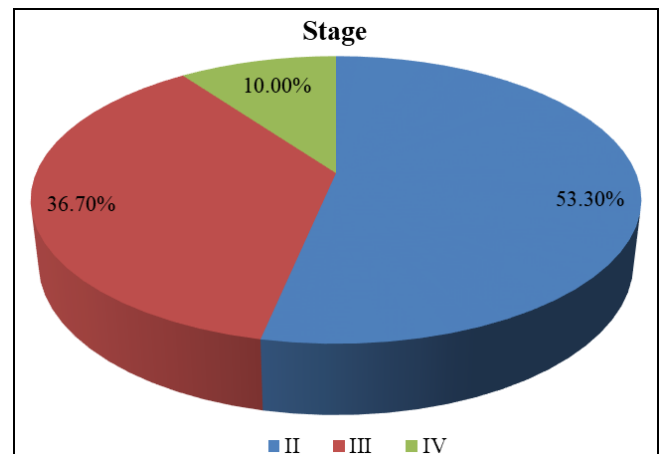


Fig 3: Pie diagram showing Stage of Tumour distribution among subjects

Table 4: HPR diagnosis distribution among subjects

		Count	%
HPR	Infiltrating Ductal Carcinoma	27	90%
	Lobular	1	3.3%
	Squamous Cell Carcinoma	2	6.7%

In the study 90% had Infiltrating Ductal Carcinoma, 6.7% had Squamous Cell Carcinoma and 3.3% had Lobular carcinoma.

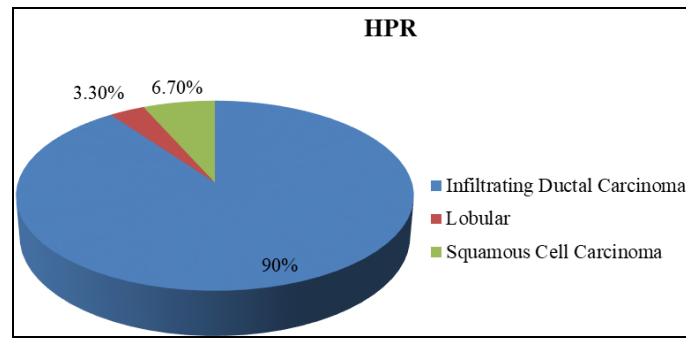


Fig 4: Pie diagram showing HPR diagnosis distribution among subjects

Table 5: Clinical Staging distribution among subjects

Clinical Staging	Count		%	
	Count	%	Count	%
T2N0M0	2	6.7%		
T2N1M0	3	10.0%		
T2N2M0	2	6.7%		
T3aN1M0	1	3.3%		
T3N0M0	8	26.7%		
T3N1M0	8	26.7%		
T3N1M1	1	3.3%		
T3N2M0	3	10.0%		
T4BN1M0	1	3.3%		
T4BN1M1	1	3.3%		

In the study on Clinical staging majority of subjects were in stage T3N0M0 and T3N1M0 (26.7% respectively).

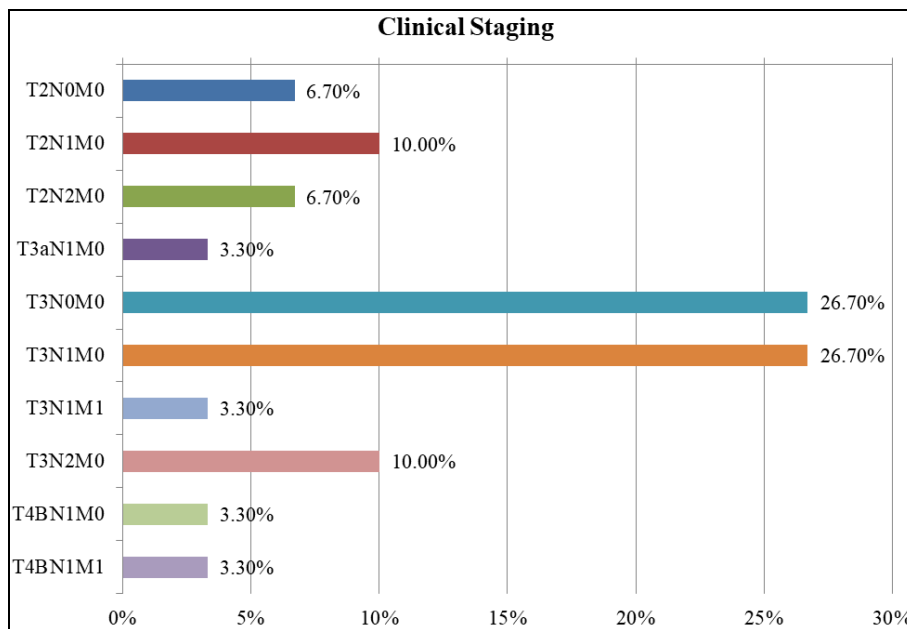


Fig 5: Bar diagram showing Clinical Staging distribution among subjects

Table 6: Neutrophil/ Lymphocyte ratio in various T stages of the tumour. Data are presented as number (percent)

N/L	T1	T2	T3	T4
1.8-2.45		2	8	
2.45-3.3		5	9	
>3.3			4	2

Table 7: Neutrophil/ Lymphocyte ratio in various N stages of the tumour. Data are presented as number (percent)

N/L	N1	N2	N3
1.8-2.45		2(6.6%)	8 (26.6%)
2.45-3.3		5(20.3)	9(30%)
>3.3			4(13.3)

Table 8: Neutrophil/ Lymphocyte ratio in various stages (total stages) of the tumour. Data are presented as number (percent)

N/L	Stage 1	Stage 2	Stage 3
< 1.8	3(10%)		
1.8-2.45	3(10%)	10(33.3%)	
2.45-3.3		6 (20%)	1 (3.33%)
>3.3		5(16.60%)	2 (6.6%)

Results

In the above study conducted in department of general surgery, 30 patients diagnosed with carcinoma breast were included. All patient’s demographic history was obtained with informed consent.

All patients were staged accordingly, blood sample were drawn for estimation of neutrophil-lymphocyte ratio before starting neoadjuvant chemotherapy and surgery. Subsequent blood samples were drawn before starting each cycle of chemotherapy. Out of 30 patients studied most common age group of presentation was between 41-50 years. 26(86.7%) post-menopausal women and 4 (13.3%) were pre-menopausal women. Patients (90%) had infiltrating ductal carcinoma as the common histological presentation, lobular was 3.3% and squamous was 2 (6.7%). In above study conducted patients in stage II 16(53.3%) were more common. Of the 30 patients studied 1 patient (3.3%) underwent (BCS) 29 (96.6%) underwent modified radical mastectomy.

2 patients had N/L ration between 1.8-2.45 with N2 nodal metastasis. 5 patients had N/L ration between 2.45-3.3 with N2, similarly 8 patients had N/L ratio between 1.8-2.45 with N3. 9 patients in 2.45 -3.3 with N3 nodes as mentioned in table 2. It was noted that patients with more lymph node metastasis also had increased neutrophil lymphocyte ratio. Patients with stage 1 disease had relatively lower N/L ratio when compared with patients in stage 2 and stage 3 disease.

Discussion

Inflammatory processes have influenced tumour growth, invasion, and metastasis. Studies have shown that increased neutrophil and lymphocyte ratio levels can play an important role in the surgery and survival rate.

In our study neutrophil-lymphocyte ratio in patients with carcinoma breast, we reviewed its relationship with the stage of the disease. According to our findings, an increase in NLR was correlated with the mortality rate. This ratio showed a significant difference in various stages of the disease. There was a significant difference between tumour size and N/L ratio with significant p value (000.5). There no significant association of N/L ration with nodal metastasis. There was significant association of N/L with staging, increased N/L was noted in increasing staging. Patient had reduced N/L with reduced tumour after chemotherapy. These findings are similar to another study done by Noh *et al.* In our study, there was a significant difference between NLR and N stage.

In a study by Koh Wha N stage and T stage were correlated with NLR; there was a significant difference between the NLR and ILC^[4].

Ozyalvacli *et al*^[5] found that preoperative high NLR was a significant diagnostic predictor of distinction of breast cancer from benign proliferative breast disease and elevated NLR was also an important prognostic marker for primary invasive breast cancer in a randomized controlled trial, and the optimal cutoff for NLR was 2.96^[5].

Chen *et al.*^[5] demonstrated that patients with NLR ≥ 2.06 showed poorer response to neoadjuvant chemotherapy and a lower pathological complete response (pCR) rate than those with NLR < 2.06 .^[6] Liu *et al.*^[6] reported that NLR is independently correlated with OS and DFS; the cutoff value of NLR (3.0) was consistent with that of most of previous studies^[7].

Dirican *et al.*^[8] focused on the performance of the preoperative NLR as a prognostic factor in 1527 patients with BC with a follow-up of nearly 6 years^[8].

Yao *et al.*^[6] found that patients with high NLR > 2.57 showed a significantly lower OS than those with lower NLR^[9].

Jia *et al.* reported that a high NLR before treatment was independently associated with a worse prognosis for BC^[10].

Conclusion

NLR is more likely to be a clinically prognostic factor in breast cancer; the low scores have invariably been shown to be deleterious in terms of tumour progression. The neutrophils and lymphocytes are routine detection index and affordable to obtain. However, we still cannot gain the identical cutoff point and the exact mechanism via previous studies. Henceforth, further feasibility studies with multi-central and a large sample size are required before it can be considered.

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