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Assessment of estrogen receptor, progesterone receptor of infiltrating ductal carcinoma of breast for neoadjuvant chemotherapy

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Abstract
Background: The aims and objectives of this study are to study the influence of Estrogen receptor ER, Progesterone receptor PR of patients having infiltrating ductal carcinoma of breast recieving Neoadjuvant chemotherapy, To study the influence of ER and PR receptors in patients receiving neoadjuvant chemotherapy & correlate complete pathological response.
Methods
- **Type of study:** Prospective clinical study. present study was carried out in the department of general surgery Vinayaka Missions medical college and hospital karaikal from July 2016 – December 2017.
- HPE (Histopathological examination) and ER PR status was done. Patients diagnosed with locally advanced breast cancer underwent simple randomization into 2 treatment groups.

Group 1: AC (Adriamycin 60mg/m2, Cyclophosphamide 600mg/m2) once every 3 weeks for 4 cycles
Group2: Docetaxel 75 mg/m2 for 4 cycles every 3 weekly(11).
Clinical examination was performed after every two cycles and completing all the chemotherapy, study group patients were subjected to Modified radical mastectomy which was then followed by evaluation of pathological response.
Conclusion: In this study 30 patients ER PR status was done. According to ER PR status Neoadjuvant chemotherapy regimen given. NCT response was assessed with clinical / imaging study. There was reduction in tumor size and change in lymph node status in both the groups with p value of .44. As our study size is small we cannot predict the actual outcome of the two study groups. We need larger sample size to predict the actual outcome.
Results: The statistical analysis was performed by STATA 11.2. Descriptive statistics of frequency and percentage were performed all the study variables. Chi square test were used to measure the association between the CP response with ER status. $P<0.05$ considered as statistically significance.

Keywords: Mammography, neoadjuvant chemotherapy, downstaging, pathological complete response, birads, modified radical mastectomy, axillary node dissection

Introduction

- Cancer is often considered as a disease of affluences but about 70% deaths due to cancer occur in the low and middle income countries.
- Leading cause of death in many wealthy countries and its toll is rising in poor regions.
- Breast cancer is a cancer that develops in the cells of breast of men and women. Worldwide breast cancer is the second most common cancer after lung cancer and fifth most common cause of cancer death.

It's a multifactorial disease. Approximately 40,000 women die of breast cancer each year. Carcinoma breast is the second commonest malignancy of females next to cervical cancer. It's responsible for about 20% of female cancer deaths.

Table 1: Comparison of Incidence and Mortality of Breast cancer in India and World in 2012(1)

Age standardized rate (per 1000000)	India	World
Incidence	25.8	43.3
Mortality	12.7	12.9

- Nowadays breast cancer is predicted largely on the result of randomized prospective clinical trials.
- Mortality in Breast cancer can be controlled by screening, neoadjuvant systemic therapy, adjuvant radiotherapy.
- Better outcomes are expected as we make a framework from investigations through new therapies. The optimal management of LABC encompasses combined-modality therapy with Neoadjuvant Chemotherapy (NACT) comprising Anthracyclines and Taxane based regimen, followed by loco regional therapy (surgery and radiation) and hormonal and targeted therapy where ever necessary (4).
- The advantages of NACT in LABC include (5) :
- Targeting distant micro metastases
- Down staging of the primary tumour, which increase the chance of resectability and also Breast Conservation surgery [BCS] whenever possible.
- In-vivo response of chemotherapy can be assessed because of increased drug delivery through intact vasculature.
- When cancer occurs in the breast of woman under forty it is more rapid in progress than when the patient is older, and also more extensive. Remote sympathy likewise takes place more readily in them than in the old, so that the operation success better in the latter on this account. – John Hunter (1728-1793)
- Breast cancer development and regression involves complex interaction between hormone receptors and transcriptional profile of ER+ PR+, ER - PR- tumors is the main discriminative factor for breast cancer phenotype, breast cancer remains more heterogenous with different phenotypes.
- The result of various different growth regulator pathways that could be activated and the possibility that virtually all signalling pathways can cross talk underlying the complexity of progression. Tumour cells are able to produce growth factors by autocrine means and frequently express several classes of growth factor receptors and their down streaming signalling elements.

Methods

The purpose of this thesis is to study and report the observations made on the cases of cancer breast in Vinayaka Missions medical college from July 2016 to august 2018.

Inclusion criteria: Newly diagnosed and histologically proven locally advanced breast carcinoma.

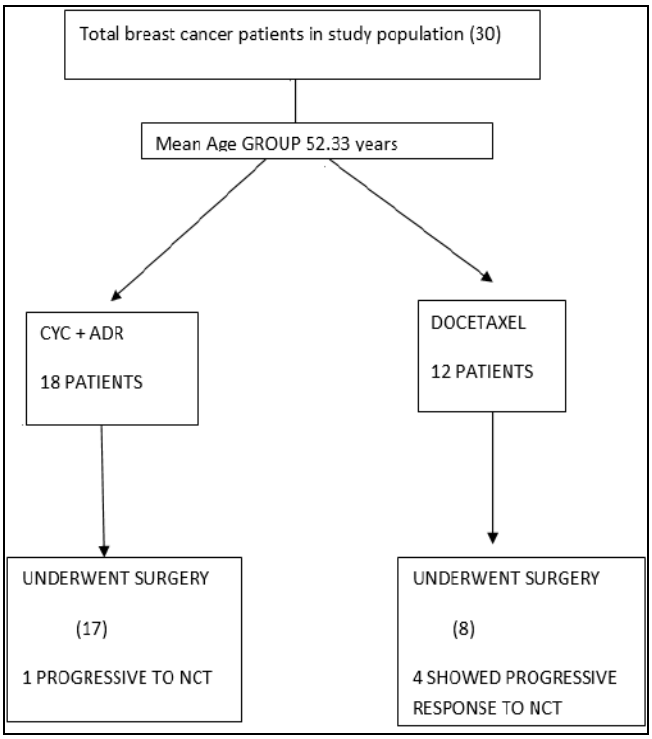
Exclusion Criteria: Diagnosis of benign breast disease, Birads 1, 2,. Male breast cancer patients, Patients with other malignancies, Pregnant women with breast cancer.

Definition of end points

Response to NACT defined as CR (Complete response), PR (Partial response), SD (Stable disease) and PD (Progressive disease) based on the RECIST criteria 1.1. Pathological complete response (pCR) defined as absence of invasive cancer component in breast and axillary lymph nodes resected specimen.

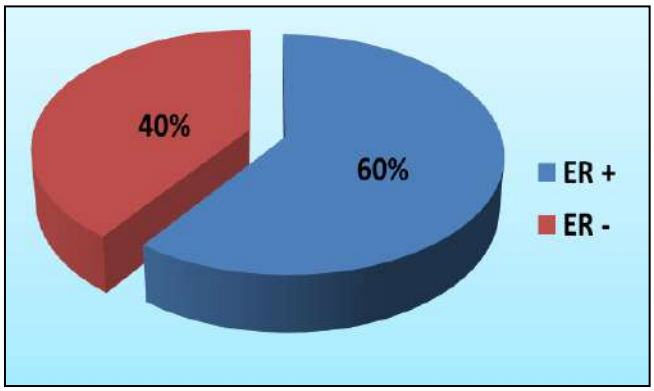
Results

Consort Diagram of Study Population



Receptor status

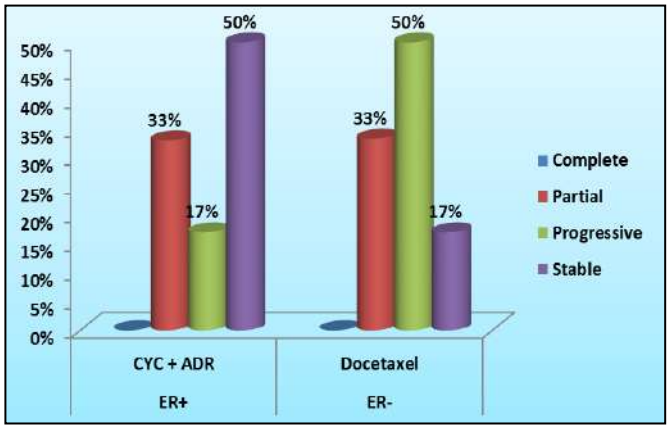
	Number of Cases	Percentage
ER +	18	60%
ER -	12	40%
Total	30	



1) Receptor status showing Number of ER+ and ER-ve individuals with pie diagram.

2) Neoadjuvant Chemotherapy cycle 1

	ER +		ER -	
	CYC + ADR	%	Docetaxel	%
Complete				
Partial	6	33.3%	4	33.3%
Progressive	3	16.67%	6	50.0%
Stable	9	50.00%	2	17%
Total	18		12	



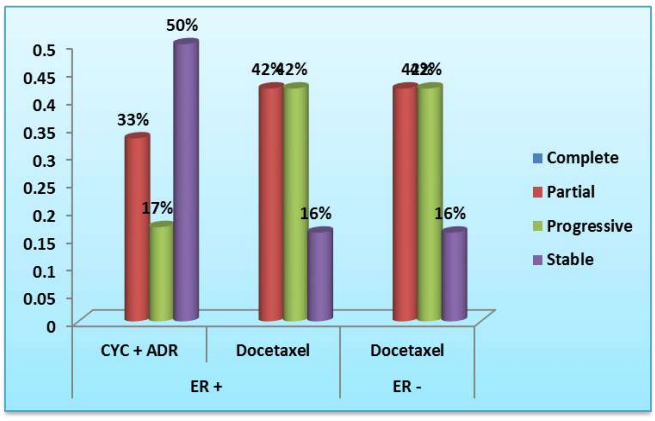
2) Bar chart and table showing Pathological response after first cycle of chemotherapy

In this study group of 30 patients 18 patients are ER+ and 12 Patients are ER –ve. The former are started with CYC+ADR and the latter are started with Docetaxel respectively. In ER +ve group out of 18, 6 patients (33%) showed partial response, 9 (50%) showed stable response, and 3 (17%) showed Progressive response.

In ER-Ve group out of 12 patients 4 (33.3%) showed partial response, 2 patients (16.67%) showed stable response and 6 patients (50%) showed progressive response.

3) Neo adjuvant chemotherapy cycle II

	ER +			ER -
	CYC + ADR	docetaxel	P-Value	Docetaxel
Complete			0.407	
Partial	7 (47%)	1 (33.3%)		5 (42%)
Progressive	1 (7%)	1 (33.3%)		5 (42%)
Stable	7 (47%)	1 (33.3%)		2 (16%)
Total	15	3		12



3) Bar chart and table showing Pathological response after Second cycle of chemotherapy

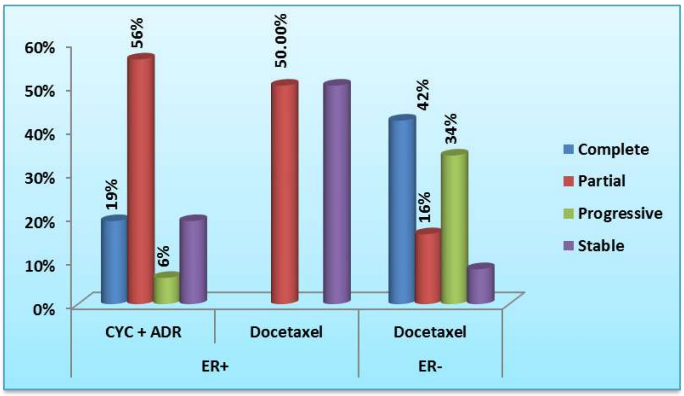
In this cycle out of 18 patients in ER + (CYC + ADR) 7 (47%) patients showed partial response, 7 (47%) showed stable response, 1 (7%) patients showed progressive response & those who were given docetaxel 1 patient (33.33%) showed partial response, 1 (33.33%) patient showed progressive response, 1 patients (33.33%) showed stable response

Out of 12 ER-ve (DOCETAXEL) patients 5 (42%) patients showed partial response 2 (16%) showed stable response and 5 (42%) showed progressive response.

4) Neoadjuvant

Chemotherapy Cycle III

	ER+			ER -	
	CYC + ADR	Docetaxel	P-Value	Docetaxel	%
Complete	3 (19%)		0.731	5	42%
Partial	9 (56%)	1 (50%)		2	16%
Progressive	1 (6%)			4	34%
Stable	3 (19%)	1 (50%)		1	8%
Total	16	2		12	



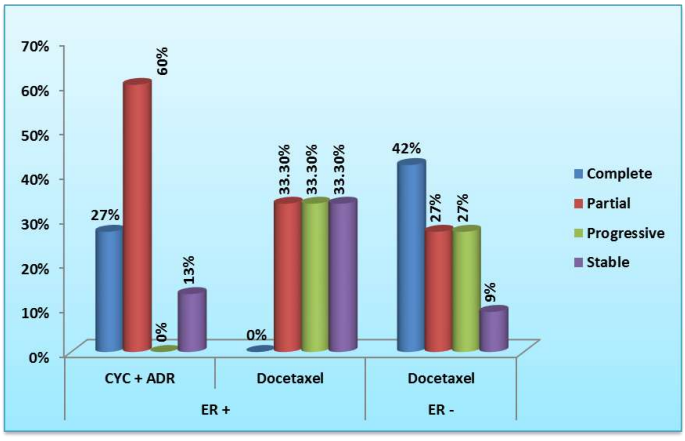
4) Bar chart and table showing Pathological response after third cycle of chemotherapy

Out of 18 ER +VE 3 (19%) showed complete response, 9 patients (56%) showed partial response, 1 patient showed progressive response,3 patients showed stable response and 1 patient who was given Docetaxel also shown Partial response. 1 patients (50%) showed stable response with Docetaxel. The p value was calculated to be.731 among the two groups.

Out of 12 ER –VE 5 (42%) showed complete response, 2 (16%) showed partial response, 1 patient (8%) showed stable response & 4 (34%) patients showed Progressive response.

5) Neoadjuvant chemotherapy cycle IV

	ER+			ER-
	CYC + ADR	Docetaxel	P-Value	Docetaxel
Complete	4 (27%)		0.081	4 (42%)
Partial	9 (60%)	1 (33.3%)		3 (27%)
Progressive		1 (33.3%)		4 (27%)
Stable	2 (13%)	1 (33.3%)		1 (9%)
Total	15	3		12



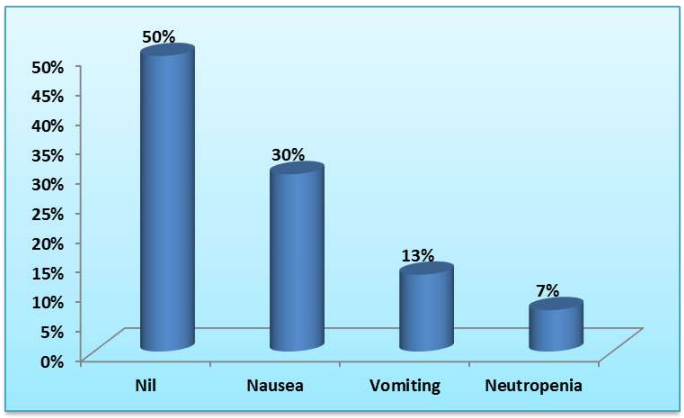
5) Bar chart and table showing Pathological response after fourth cycle of chemotherapy

In 18 ER +Ve patients, out of 15 patients who were given CYC + ADR, 4 (27%) patients showed complete response, 9 (60%) patients showed partial response, 2 (13%) patients showed stable response, In 3 Patients who were given DOCETAXEL 1 (33.33%) showed complete response, 1 (33.33%) showed partial response, and 1 patient (33.33%) showed progressive response.P value was noted to be.081

In 12 ER-ve patients who were given DOCETAXEL 5 patients (42%) showed complete response, 3 (27%) showed partial response, 1 patient (9%) showed stable response. 3 patients (27%) showed progressive response.

6) Adverse Reactions after four cycles of chemotherapy

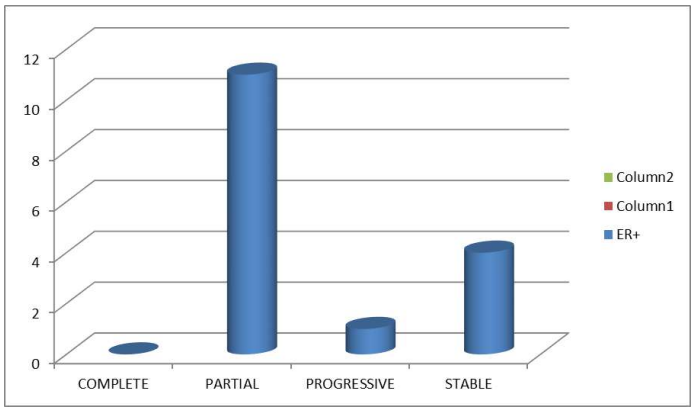
	Number	%
Nil	15	50%
Nausea	9	30%
Vomiting	4	13%
Neutropenia	2	7%



Out of the 30 patients 15 patients were asymptomatic and 15 patients showed adverse reactions. Out of them 9 patients 30% gave complaints of nausea and 4 patients (13%) gave complaints of vomiting. 2 patients (7%) had neutropenia.

7) ER+ve: Pathological response

complete	
partial	11 (64%)
stable	4 (13.33%)
progressive	1 (3.33%)
total	17

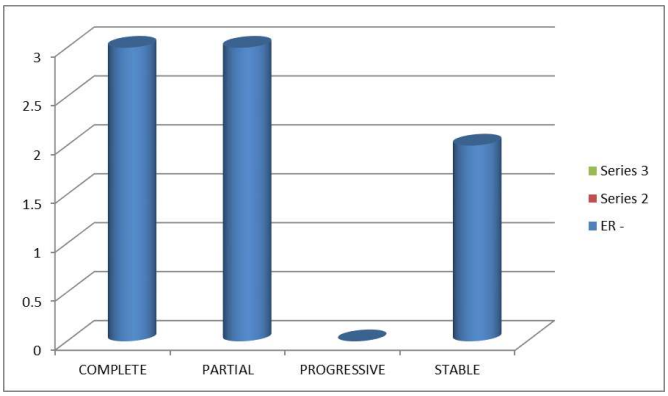


7) Bar diagram showing Pathological response in ER+ ve patients

In ER +ve patients 11 patients showed partial response, 4 patients showed stable response and 1 patients showed progressive response.

8) ER-VE Pathological Response

Complete	3 (37.5%)
Partial	3 (37.5%)
Stable	2 (25%)
Progressive	0
Total	8



8) Bar diagram showing pathological response in ER –ve individuals

In ER _ve patients 3 (37.5%) showed complete response, 3 (37.5%) showed partial response and 2 (25%) showed stable response.

Conclusion

- In this prospective hospital based study conducted in vinayaka mission medical college and hospital in the department of general surgery, we access the ER and PR of infiltrating ductal carcinoma of breast for neoadjuvant chemotherapy.
- We selected 40 patients with ca breast. 30 patients were selected according to inclusion and exclusion criteria with infiltrating ductal carcinoma. In that total study population, 18 were given cyclophosphamide and adyriamycin chemotherapy regimen out of them those patients who didn't respond to CYC +ADR drug was changed to Docetaxel. In second group 12 patients were given docetaxel.
- Out of 18 patients in the first group 3 patients were not responded to adriamycin and cyclophosphamide, and the drug was changed to Docetaxel, out of this three patients 1 patient not responded to Docetaxel and was not operated. Other patients who underwent neoadjuvant therapy were operated.
- Out of 12 patients in group II 8 patients responded to neoadjuvant chemotherapy with Docetaxel and 4 patients showed progressive response and, the other patients were operated. Out of the 30 patients 15 patients were asymptomatic and 15 patients showed adverse reactions. Out of them 9 patients 30% gave complaints of nausea and 4 patients (13%) gave complaints of vomiting. 2 patients (7%) had neutropenia.
- Funding: No funding sources
- Conflict of interest: None declared
- Ethical approval: The study was approved by the Institutional Ethics Committee

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