ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Neoadjuvant Chemotherapy With Trastuzumab In Locally Advanced Breast Cancer -Pathological Response Rate, Predictive And Prognostic Factors.

P Sumathi[1]*, Ganganesamy[2], and M Preethi Saratha[3].

[1]Professor, Department Of General Surgery, Government Mohan Kumara Mangalam Medical College & Hospital, Salem, Tamil Nadu India.
[2]Assistant Professor, Department Of General Surgery, Government Mohan Kumara Mangalam Medical College & Hospital, Salem, Tamil Nadu India.
[3]Final year Post Graduate, Department Of General Surgery, Government Mohan Kumara Mangalam Medical College & Hospital, Salem, Tamil Nadu India.

ABSTRACT

HER2-positive breast cancer (BC) accounts for 20–25% of cases and is associated with an aggressive clinical course. Trastuzumab, a monoclonal antibody targeting HER2, improves outcomes in these patients. This study evaluates neoadjuvant chemotherapy with trastuzumab in HER2-positive locally advanced BC. This prospective study was done with 50 patients with HER2-positive BC, treated with neoadjuvant chemotherapy and trastuzumab at GMKMCH from 2022 to 2024. The mean age was 57.1 years (SD = 7.1). Invasive carcinoma was the most common diagnosis (33.33%). Clinical stages included stage IIIB (32%) and IIB (28%). Hormone receptor status showed 44% ER and PR positive. Treatment resulted in a 60% complete response and 40% partial response. Clinical parameters were normal, with mean hemoglobin 12.3 g/dL, blood urea 25.0 mg/dL, and serum creatinine 0.96 mg/dL. Neoadjuvant chemotherapy with trastuzumab is effective in HER2-positive BC, demonstrating high response rates and good systemic health outcomes. Further research is needed to identify long-term impacts and predictive markers.

Keywords: HER2-positive breast cancer, trastuzumab, neoadjuvant chemotherapy, pathological response, hormone receptor status, treatment outcomes, invasive carcinoma.

https://doi.org/10.33887/rjpbcs/2025.16.2.4

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Breast cancer (BC) remains the most prevalent cancer among women globally, accounting for 2.26 million new cases annually, with HER2-positive BC representing 20–25% of all cases, often associated with an aggressive clinical course and poor prognosis [1, 2]. Trastuzumab, a humanized monoclonal antibody targeting HER2, has revolutionized treatment outcomes by improving disease-free survival (DFS), overall survival (OS), and response rates in HER2-positive BC patients. Its anti-tumor mechanisms include inhibiting HER2-driven cell signaling, reducing cell proliferation, restoring apoptosis via the PI3K/Akt pathway, and preventing HER2-regulated angiogenesis [3]. Additionally, trastuzumab enhances chemotherapy sensitivity and stimulates immune responses through antibody-dependent cellular cytotoxicity (ADCC), mediated by natural killer cells [4]. The genetic polymorphism FCGR3A-V158F has been identified as a critical factor influencing the efficacy of trastuzumab, with variations affecting ADCC potency and patient responses. Despite its efficacy, resistance to trastuzumab remains a significant challenge in advanced HER2-positive BC, prompting the development of novel therapeutic approaches, such as next-generation antibody-drug conjugates like trastuzumab emtansine (T-DM1) and trastuzumab deruxtecan (T-DXd), which have demonstrated improved outcomes [5]. The study focuses on neoadjuvant chemotherapy with trastuzumab in HER2-positive locally advanced breast cancer, emphasizing pathological response rates, and predictive, and prognostic factors.

MATERIAL AND METHODS

This prospective study was conducted in the Department of General Surgery, GMKMCH, from 2022 to 2024, involving 50 purposively sampled carcinoma breast cases. Inclusion criteria encompassed locally advanced, inoperable, inflammatory, and early breast carcinoma with HER2NEU+ status, while patients with cardiac illness were excluded. Clinical diagnosis included investigations such as hemogram, renal and liver function tests, blood sugar levels, urine routine, HIV, HBsAg, and VDRL screening, FNAC, trust biopsy, USG of the breast and axilla, metastatic workup (CECT chest, abdomen, MRI spine), and hormone receptor studies. Data on age, demographics, socioeconomic status, and clinical history were collected after obtaining informed consent. Patients were followed up from admission through discharge and periodically, with data analyzed using statistical software.

RESULTS

The study included middle-aged to elderly patients, with a mean age of 57.1 years (Table 1). Invasive carcinoma was the most common type, accounting for 33.33% of cases (Table 2), with all patients being HER2-positive, making them eligible for trastuzumab therapy. Regarding hormone receptor status (Table 3), 44% were both ER and PR positive, while 36% were ER positive but PR negative. Clinical stages (Table 4) showed that the majority of patients presented at advanced stages: stage IIIB (32%), stage IIB (28%), and stage IIA (20%). Treatment responses (Figure 1) were favorable, with 60% achieving complete responses and 40% showing partial responses. Clinical parameters (Table 5) indicated no significant issues, with a mean hemoglobin level of 12.3 g/dL, mean blood urea of 25.0 mg/dL, serum creatinine of 0.96 mg/dL, and normal liver function in 96% of patients. Blood sugar levels were within normal ranges: random 117.1 mg/dL, fasting 90.0 mg/dL, and postprandial 145.0 mg/dL. These findings suggest that despite the advanced stages of cancer, patients were generally in good systemic health, which may have contributed to the positive treatment responses.

Table 1: Demographics and Clinical Data (n=50).

Parameter	Value	Standard Deviation
Mean Age	57.1 years	7.1 years
Age Distribution	40-49 years: 20%	
	50-59 years: 30%	
	60-69 years: 30%	
	70-79 years: 20%	

ISSN: 0975-8585

Table 2: Diagnosis and HER2 Status (n=50).

Diagnosis Type	Number of Patients	Percentage
Invasive Carcinoma	20	33.33%
Ductal Carcinoma	10	16.67%
Invasive Lobular Carcinoma	10	16.67%
Mixed Ductal Carcinoma	6	10.00%
Inflammatory Breast Carcinoma	4	6.67%
HER2 Status	**50**	**100%**

Table 3: Hormone Receptor Status (n=50).

Receptor Status	Number of Patients	Percentage
ER Positive, PR Positive	22	44%
ER Positive, PR Negative	18	36%
ER Negative, PR Positive	6	12%
ER Negative, PR Negative	4	8%

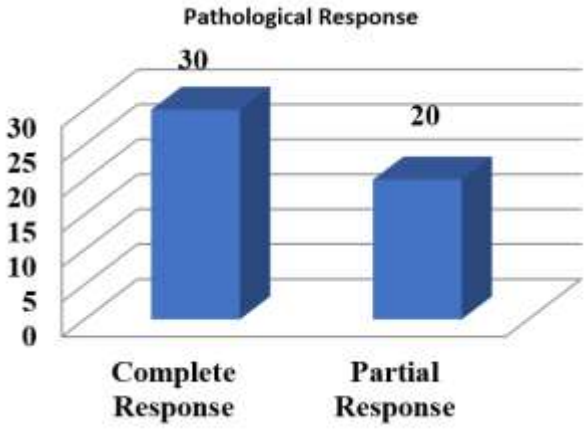
Table 4: Clinical Stage (n=50).

Clinical Stage	Number of Patients	Percentage
Stage IIA	10	20%
Stage IIB	14	28%
Stage IB	16	32%
Stage IC	10	20%

Table 5: Clinical Investigations (n=50).

Investigation Parameter	Mean/Value	Standard Deviation
Complete Hemogram:		
- Hemoglobin (HB)	12.3 g/dL	0.8 g/dL
Blood Urea	25.0 mg/dL	4.2 mg/dL
Serum Creatinine	0.96 mg/dL	0.1 mg/dL
Liver Function Test	96% normal, 4% elevated	
Blood Sugar:		
- RBS (Random Blood Sugar)	117.1 mg/dL	9.1 mg/dL
- FBS (Fasting Blood Sugar)	90.0 mg/dL	5.0 mg/dL
- PPBS (Postprandial Blood Sugar)	145.0 mg/dL	10.5 mg/dL

Figure-1: Pathological Response.



DISCUSSION

This prospective study aimed to evaluate the pathological response to neoadjuvant chemotherapy combined with trastuzumab in patients with HER-2 positive breast cancer, alongside identifying predictive and prognostic markers that could influence treatment outcomes. Conducted in the Department of General Surgery at GMKMCH from 2022 to 2024, the study involved 50 purposively sampled cases of carcinoma breast, all of which were HER-2 positive. The study's findings shed light on the potential effectiveness of this combined treatment regimen and contribute to the growing body of evidence in the management of HER-2-positive breast cancer.The mean age of the patients was 57.1 years, with a standard deviation of 7.1 years. This indicates a study population that was predominantly middle-aged to elderly, as breast cancer incidence is known to increase with age. The age distribution shows that 30% of the patients were between 50-59 years and 60-69 years, with 20% in both the 40-49- and 70-79-years age ranges. These findings are in line with the epidemiological trends showing that breast cancer predominantly affects women over 50 years of age. This underscores the importance of age as a risk factor in breast cancer, with older women more likely to present with advanced disease at diagnosis. According to Miao He et al. (2024) [1], the study population had a median age of 51 years, with a broad age range spanning from 21 to 74 years, indicating a diverse cohort that included both younger and older individuals. Regarding the types of carcinoma, invasive carcinoma was the most common, accounting for 33.33% of cases. This is consistent with the literature, as invasive ductal carcinoma (IDC) is the most frequently diagnosed breast cancer subtype, contributing to the majority of breast cancer diagnoses globally (Gopal Menon et al., 2024) [6]. Jan Paredes Mogica et al. (2023) [7] reported that 92.3% (96/104) of the patients had invasive ductal carcinoma, making it the most prevalent histological type in their study. This finding underscores the high incidence of invasive ductal carcinoma, which is known for its aggressive nature and ability to spread beyond the milk ducts to surrounding tissues. The predominance of this type of carcinoma aligns with numerous other studies that have shown it to be the most common form of breast cancer, further reinforcing the need for targeted diagnostic and therapeutic strategies for this subtype. The next most common subtypes were ductal carcinoma (16.67%) and invasive lobular carcinoma (16.67%), while mixed ductal carcinoma and inflammatory breast carcinoma were less frequent, constituting 10% and 6.67%, respectively. These subtypes reflect the heterogeneity of breast cancer, where IDC is the predominant subtype, but lobular carcinoma and inflammatory breast cancer also represent a significant portion of cases, each with distinct prognostic and treatment implications. The HER-2 positive status was found in all patients, which is a crucial finding, as HER-2 positive breast cancer is known to have a more aggressive biological behavior but also responds well to targeted therapies like trastuzumab. Trastuzumab targets the overexpression of the HER-2 protein and has been shown to significantly improve survival outcomes in HER-2-positive breast cancer. The study revealed that 44% of the patients were positive for both estrogen and progesterone receptors (ER+ PR+), suggesting that they may benefit from hormonal therapy, such as aromatase inhibitors or tamoxifen. A further 36% were ER+ PR-, indicating that while these patients are likely to benefit from endocrine therapy targeting the estrogen receptor, the lack of PR expression could potentially make the cancer more aggressive and less responsive to hormonal treatments. The remaining 20% of patients were ER- PR- or ER+ PR+, highlighting that a subset of patients may not respond to hormonal therapy and may need alternative approaches. In the study by Abigail S. Caudle et al. (2010) [8], among the 224 patients with ER- or PR-positive, HER2-positive tumors, only two patients (0.9%) experienced progressive disease (PD). In contrast, 16 out of 882 patients (1.8%) with ER- or PR-positive, HER2-negative tumors had PD. In the triple-negative subgroup (n=167), which included ER-, PR-, and HER2-negative tumors, seven patients (4%) developed PD. Notably, PD occurred in only one (0.7%) of 148 HER2-positive patients who received trastuzumab-containing regimens, whereas eight (3.3%) of 243 HER2-positive patients who received neoadjuvant chemotherapy (NCT) without trastuzumab experienced PD, indicating the significant impact of trastuzumab on reducing the risk of PD in HER2-positive patients. Regarding the clinical stages, the majority of patients presented at advanced stages of the disease, with 32% in stage IIIB and 20% in stage IIIC. This finding correlates with the aggressive nature of HER-2-positive breast cancer, which is often diagnosed at later stages. According to Wenjin Yin et al. (2022) [9], the majority of patients were diagnosed at clinical stage III, accounting for 73.58% of the cases, indicating a high prevalence of locally advanced disease at the time of diagnosis. This suggests that a significant portion of the patient population may have experienced delayed detection or progression of the disease, which could impact treatment outcomes and prognosis. In terms of pathological response to neoadjuvant chemotherapy combined with trastuzumab, 60% of patients achieved a complete response, and 40% showed a partial response. In the study by Dong Hui Cho et al. (2013) [10], pathologic complete response (pCR) was achieved in 13 out of 28 patients, highlighting a notable proportion of patients who experienced complete eradication of the tumor following treatment. Additionally, Laurent Arnould et al. (2007) [11] found that the pathologic

complete response rate was significantly higher in low- and high-amplification tumors compared to no-amplification tumors, with rates of 44% versus 6%, respectively (P < 0.004). Furthermore, the pCR rate was significantly higher in high-amplification tumors (56%) compared to low-amplification tumors (22%) (P < 0.005), indicating that tumor amplification may play a critical role in predicting treatment response and achieving better outcomes.The clinical investigations conducted on the patients revealed that their systemic health was generally stable. The mean hemoglobin level of 12.3 g/dL, within normal limits, indicates that there were no significant issues with anemia, which is important as anemia can interfere with treatment tolerance and quality of life in cancer patients. The blood urea and serum creatinine levels were also within normal limits (25.0 mg/dL and 0.96 mg/dL, respectively), suggesting that renal function was well-preserved, an essential factor for the safe administration of chemotherapy drugs that are metabolized by the kidneys. Liver function tests were normal in 96% of the patients, confirming that hepatic function was not compromised, which is crucial given the potential hepatotoxicity of some chemotherapy agents. Blood sugar levels, including random (117.1 mg/dL), fasting (90.0 mg/dL), and postprandial (145.0 mg/dL) values, were also within normal ranges, though some patients exhibited slight hyperglycemia. This is an important consideration, as some chemotherapy agents can affect glucose metabolism, and patients may be at risk of developing diabetes or glucose intolerance during treatment. Monitoring blood glucose levels in these patients is essential for timely intervention. This study, while informative, has several limitations that should be acknowledged. Firstly, the sample size of 50 patients may be relatively small, potentially limiting the generalizability of the findings to the broader population of HER2-positive breast cancer patients. Additionally, the study was conducted at a single center, which may introduce regional biases. The follow-up duration was limited to the treatment period and short-term post-treatment, so the long-term effects and recurrence rates of neoadjuvant chemotherapy with trastuzumab could not be fully assessed. Another limitation is the exclusion of patients with cardiac illness, which may have impacted the generalizability of the findings to those with pre-existing cardiac conditions, who are also often treated with trastuzumab. Furthermore, the reliance on clinical investigations and imaging studies, rather than histopathological confirmation at all follow-up stages, may introduce some level of diagnostic variability. Future studies should consider increasing the sample size and conducting multi-center trials to ensure the findings are more broadly applicable across different populations. Long-term follow-up studies should be conducted to assess the durability of the pathological response, survival outcomes, and recurrence rates post-treatment. Additionally, exploring the effectiveness of neoadjuvant chemotherapy with trastuzumab in patients with comorbidities, including cardiac conditions, would be beneficial to understand how these factors influence treatment efficacy and safety. Future research should also focus on identifying more specific predictive biomarkers, including genetic and molecular markers, to guide personalized therapy. Lastly, randomized controlled trials comparing different regimens involving trastuzumab could provide stronger evidence for optimizing treatment strategies in HER2-positive breast cancer.

CONCLUSION

In conclusion, this study demonstrated that neoadjuvant chemotherapy combined with trastuzumab is a highly effective treatment regimen for HER-2-positive breast cancer, with significant pathological response rates and favorable systemic health outcomes in patients. The high rate of complete responses and the relative preservation of organ function indicate that this approach can lead to improved survival outcomes. Further research is needed to explore the long-term impact of this treatment strategy and identify additional predictive markers that may guide individualized treatment plans.

REFERENCES

[1] He M, Zhao W, Wang P, Li W, Chen H, et al. Efficacy and safety of Trastuzumab Emtansine in treating human epidermal growth factor receptor 2-positive metastatic breast cancer in Chinese population: a real-world multicenter study. Front Med (Lausanne) 2024; 11:1383279.

[2] Foukakis T, Naume B, Karakatsanis A, Andersson A, Barnekow E, Edman Kessler L, et al. 339TiP - A randomized trial of trastuzumab deruxtecan and biology-driven selection of neoadjuvant treatment for HER2-positive breast cancer (ARIADNE). Ann Oncol 2024; 35(2 Suppl):S349-S356.

[3] Guarneri V, Dieci MV, Barbieri E, Piacentini F, Omarini C, et al. Loss of HER2 positivity and prognosis after neoadjuvant therapy in HER2-positive breast cancer patients. Ann Oncol 2013; 24(12):2990-4.

[4] Lemieux J, Clemons M, Provencher L, et al. The role of neoadjuvant HER2-targeted therapies in HER2-overexpressing breast cancers. Curr Oncol 2009; 16(5):48-57.

[5] Abdel-Wahed MA, Sabbour GS, Hamed AI, et al. FCGR3A V158F gene polymorphism and trastuzumab response in HER2-positive breast cancer patients. Sci Rep 2024; 14:26037.
[6] Menon G, Alkabban FM, Ferguson T. Breast Cancer. [Updated 2024 Feb 25]. In: StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2025 Jan-.
[7] Mogica JP, Tang H, Liang Y, et al. Prognostic impact of reduced HER2 protein expression in post-neoadjuvant therapy resection specimens: A single institution experience and review of the literature. Breast 2023; 72:103586.
[8] Caudle AS, Gonzalez-Angulo AM, Hunt KK, et al. Predictors of tumor progression during neoadjuvant chemotherapy in breast cancer. J Clin Oncol 2010; 28(10):1821-1828.
[9] Yin W, Wang Y, Wu Z, et al. Neoadjuvant trastuzumab and pyrotinib for locally advanced HER2-positive breast cancer (NeoATP): Primary analysis of a phase II study. Clin Cancer Res 2022; 28(18):3677-3685.
[10] Cho DH, Lee SK, Kim S, et al. Neoadjuvant human epidermal growth factor receptor-2 targeted therapy in patients with locally advanced breast cancer. J Korean Surg Soc 2013; 84(5):273-280.
[11] Arnould L, Arveux P, Couturier J, et al. Pathologic complete response to trastuzumab-based neoadjuvant therapy is related to the level of HER-2 amplification. Clin Cancer Res 2007; 13(21):6404.