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Effect Of Trastuzumab In HER2-Positive Breast Cancer Patients

Hossain MRZ[1], Mollah NU[2], Nahar S[3], Haque MS[4], Uddin MJ[5]

[1]*Dr. Mohammad Rifat Zia Hossain, Assistant Professor, Department Of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

[2]*Dr. Nazir Uddin Mollah, Professor, Department Of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

[3]*Dr. Samsun Nahar, Assistant Professor, Department Of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

[4]*Dr. Md. Saidul Haque, Medical Officer, Assistant Professor, Department Of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

[5]*Dr. Md. Jamal Uddin, Assistant Professor, Assistant Professor, Department Of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

Abstract

Background: *HER2-positive breast cancer is an aggressive subtype characterized by the overexpression of the HER2 receptor, associated with poor prognosis. Trastuzumab, a targeted therapy, has significantly improved outcomes for these patients. This study aims to evaluate the clinical characteristics, treatment responses, and hematological changes in HER2-positive breast cancer patients undergoing adjuvant trastuzumab therapy.*

Methods: *This retrospective observational study was conducted at the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from January 2023 to December 2023. The study included 30 HER2-positive breast cancer patients who received trastuzumab every three weeks as adjuvant chemotherapy. Baseline and post-treatment clinical parameters were collected and analyzed.*

Results: *The study cohort comprised 43.33% of patients aged 41-50 years, with 83.33% having the left breast impacted. Baseline clinical parameters showed a mean hemoglobin level of 11.06±1.03 g/dL, neutrophil percentage of 64.00±9.49%, leukocyte count of 23.47±3.29, and platelet count of 2.34±0.57 x 10^5/µL. Post-treatment, there was a statistically significant decrease in hemoglobin levels (mean difference of 0.54828 g/dL, p=0.002) and platelet counts (mean difference of 0.279 x 10^5/µL, p=0.004), while neutrophil and leukocyte counts showed no significant changes. Tumor sizes and lymph node metastasis rates remained largely unchanged, with 43.33% of patients at stage IIIA. Additionally, 86.67% of patients received combined hormone therapy with trastuzumab.*

Conclusion: *The study confirms the efficacy of trastuzumab in managing HER2-positive breast cancer but highlights the need for continuous hematological monitoring due to significant decreases in hemoglobin and platelet levels post-treatment. Integrating hormone therapy with trastuzumab remains crucial for improving treatment outcomes. Further research is needed to optimize therapeutic protocols and enhance patient care in this aggressive breast cancer subtype.*

Keywords: *HER2-Positive Breast Cancer, Trastuzumab, Hematological Parameters, Hormone Therapy, Treatment Outcomes*

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I. Introduction

Breast cancer remains a leading cause of morbidity and mortality among women globally, representing a significant public health concern. According to the World Health Organization (WHO), breast cancer accounts for approximately 24.5% of all cancer cases globally, with over 2.3 million new cases reported in 2020 (1). HER2-positive breast cancer, characterized by the overexpression of the human epidermal growth factor receptor 2 (HER2), constitutes about 15-20% of all breast cancer cases and is associated with aggressive tumor behavior and poor prognosis (2). The advent of HER2-targeted therapies, particularly trastuzumab, has significantly altered the landscape of treatment and improved outcomes for patients with this subtype of breast

cancer. HER2 receptors play a critical role in the progression of certain breast cancers. The overexpression of HER2 receptors leads to increased cell proliferation, survival, and metastasis, contributing to the aggressive nature of HER2-positive breast cancer (3). HER2-positive tumors are more likely to grow quickly and are less responsive to hormone therapy, resulting in a poorer prognosis compared to HER2-negative tumors (4). Clinical studies have demonstrated that the overexpression of HER2 is a significant predictor of both disease-free survival (DFS) and overall survival (OS), highlighting the necessity for effective targeted therapies (5). Trastuzumab, a monoclonal antibody targeting the HER2 receptor, was developed to address this aggressive subtype of breast cancer. It binds to the extracellular domain of the HER2 receptor, inhibiting downstream signaling pathways that promote tumor growth and survival (6). Additionally, trastuzumab mediates antibody-dependent cellular cytotoxicity, further enhancing its anti-tumor effects (7). The development of trastuzumab has revolutionized the treatment of HER2-positive breast cancer, as evidenced by several landmark clinical trials. The HERceptin Adjuvant (HERA) trial, a pivotal study, demonstrated that one year of trastuzumab after adjuvant chemotherapy significantly improved DFS and OS in women with HER2-positive early breast cancer (8). The trial reported a 10-year DFS rate of 69% for the trastuzumab group compared to 63% for the observation group (9). Another critical study, conducted by Piccart-Gebhart et al., confirmed the substantial benefits of trastuzumab, showing an absolute benefit in DFS at two years of 8.4 percentage points (10). These studies collectively highlight the efficacy of trastuzumab in improving survival outcomes for HER2-positive breast cancer patients. However, the administration of trastuzumab is not without its challenges, particularly concerning its adverse effects. Cardiotoxicity is a well-documented side effect of trastuzumab, with studies reporting a 1-4% incidence of symptomatic heart failure and a 10% incidence of substantial declines in left ventricular ejection fraction (LVEF) (11). The risk of cardiotoxicity is heightened when trastuzumab is used in combination with anthracyclines, necessitating vigilant cardiac monitoring (12). Sengupta et al. highlighted the need for regular assessment of cardiac function to manage and mitigate these risks effectively (13). In developing countries, the implementation of trastuzumab therapy faces additional hurdles, primarily related to cost, accessibility, and healthcare infrastructure. High costs and limited healthcare resources often restrict access to trastuzumab, leading to disparities in treatment outcomes (14). In Iran, for instance, the financial burden on patients and the government has prompted the development of national programs to manage trastuzumab use more effectively (15). Similar challenges are observed in other low- to middle-income countries, where high-cost drugs like trastuzumab are not universally available (16). These barriers highlight the necessity for strategies to improve drug access and affordability in resource-limited settings. Bangladesh, as a developing country, faces similar challenges in implementing trastuzumab therapy. Although specific data on the prevalence of HER2-positive breast cancer in Bangladesh is limited, the country's healthcare infrastructure and economic constraints likely mirror the barriers observed in other developing nations. Enhancing access to trastuzumab in Bangladesh will require concerted efforts to address financial, logistical, and infrastructural challenges. Studies from neighboring countries, such as India, indicate that the availability of biosimilar trastuzumab has improved access and outcomes, suggesting a potential pathway for similar improvements in Bangladesh (17). In conclusion, while trastuzumab has significantly improved the prognosis for HER2-positive breast cancer patients globally, its implementation in developing countries like Bangladesh is fraught with challenges. Addressing these barriers is crucial to ensuring that all patients, regardless of geographic and economic constraints, can benefit from this life-saving therapy.

II. Methods

This retrospective observational study was conducted at the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The study duration was from January 2023 to December 2023. The sample comprised 30 patients diagnosed with HER2-positive breast cancer. Patients were selected based on their HER2-positive status confirmed by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH). Patients requiring surgical management were excluded from the study to maintain homogeneity in the treatment regimen. The primary indication for trastuzumab administration was as adjuvant chemotherapy. Each patient received trastuzumab at a dose of 8 mg/kg as a loading dose followed by 6 mg/kg every three weeks. Data on patient demographics, treatment regimens, adverse effects, and clinical outcomes were collected from medical records. Follow-up data were gathered for assessing disease-free survival (DFS) and overall survival (OS). Cardiac function was monitored through regular echocardiograms to assess left ventricular ejection fraction (LVEF), given the known cardiotoxicity associated with trastuzumab. All collected data were analyzed using statistical software to determine the efficacy and safety profile of trastuzumab in this cohort. Ethical approval for the study was obtained from the institutional review board of Dhaka Medical College and Hospital, and all patient information was anonymized to ensure confidentiality.

III. Results

Table 1: Distribution of participants by baseline characteristics (N=30)

Baseline Characteristics	n	%
Age		
<=40	7	23.33%
41-50	13	43.33%
51-60	3	10.00%
>60	7	23.33%
Impacted Breast		
Left Breast	25	83.33%
Right Breast	5	16.67%
Clinical Parameters		
Hemoglobin	11.06±1.03	
Neutrophil	64.00±9.49	
Leukocytes	23.47±3.29	
Platelet (*10^5)	2.34±0.57	

The study included 30 HER2-positive breast cancer patients with varying baseline characteristics. The age distribution of participants was as follows: 7 patients (23.33%) were aged 40 years or younger, 13 patients (43.33%) were aged between 41 and 50 years, 3 patients (10.00%) were aged between 51 and 60 years, and 7 patients (23.33%) were older than 60 years. Regarding the impacted breast, a significant majority of the cases involved the left breast, with 25 patients (83.33%) affected, while the right breast was impacted in 5 patients (16.67%). The clinical parameters recorded at baseline included an average hemoglobin level of 11.06±1.03 g/dL, a neutrophil percentage of 64.00±9.49%, leukocytes count of 23.47±3.29 (units unspecified), and a platelet count of 2.34±0.57 x 10^5/μL.

Table 2: Distribution of tumor related characteristics among the participants (N=30)

Variables	n	%
Size of Tumor		
T1b	0	0.00%
T1c	12	40.00%
T2	8	26.67%
T3	10	33.33%
Lymph Node Metastasis		
Positive	26	86.67%
Negative	4	13.33%
Tumor Staging		
I	3	10.00%
IIA	10	33.33%
IIB	4	13.33%
IIIA	13	43.33%
Hormone Receptor Status		
ER+ and PgR+	26	86.67%
ER- and PgR-	4	13.33%

The distribution of tumor-related characteristics among the 30 participants revealed a varied profile. In terms of tumor size, no patients had T1b tumors, while 12 patients (40.00%) had T1c tumors, 8 patients (26.67%) had T2 tumors, and 10 patients (33.33%) had T3 tumors. Lymph node metastasis was prevalent in the majority of participants, with 26 patients (86.67%) showing positive lymph node involvement, and 4 patients (13.33%) exhibiting no lymph node metastasis. Tumor staging indicated that 3 patients (10.00%) were at stage I, 10 patients (33.33%) were at stage IIA, 4 patients (13.33%) were at stage IIB, and 13 patients (43.33%) were at stage IIIA. Regarding hormone receptor status, a substantial proportion of the participants, 26 patients

(86.67%), were both estrogen receptor (ER) positive and progesterone receptor (PgR) positive, while 4 patients (13.33%) were both ER negative and PgR negative.

Table 3: Distribution of participants by treatment combination with hormone therapy (N=30)

Combined Hormone Therapy	n	%
Yes	26	86.67%
No	4	13.33%

26 out of the 30 participants (86.67%) were treated with hormone therapy in addition to trastuzumab, while 4 patients (13.33%) did not receive any combined hormone therapy.

Table 4: Tumor related parameters at post-treatment follow-up (N=30)

Tumor related parameters	n	%
Size of Tumor		
T1b	2	6.67%
T1c	12	40.00%
T2	6	20.00%
T3	10	33.33%
Lymph Node Metastasis		
Positive	26	86.67%
Negative	4	13.33%
Tumor Staging		
I	4	13.33%
IIA	11	36.67%
IIB	2	6.67%
IIIA	13	43.33%
Hormone Receptor Status		
ER+ and PgR+	27	90.00%
ER- and PgR-	3	10.00%

The tumor-related parameters at post-treatment follow-up for the 30 participants showed notable findings. In terms of tumor size, 2 patients (6.67%) had T1b tumors, 12 patients (40.00%) had T1c tumors, 6 patients (20.00%) had T2 tumors, and 10 patients (33.33%) had T3 tumors after treatment. The status of lymph node metastasis remained consistent with the baseline findings, with 26 patients (86.67%) still showing positive lymph node involvement and 4 patients (13.33%) having no lymph node metastasis. Post-treatment tumor staging indicated slight improvements, with 4 patients (13.33%) at stage I, 11 patients (36.67%) at stage IIA, 2 patients (6.67%) at stage IIB, and 13 patients (43.33%) at stage IIIA. The hormone receptor status at follow-up revealed that 27 patients (90.00%) were ER positive and PgR positive, while 3 patients (10.00%) were ER negative and PgR negative.

Table 5: Mean±SD clinical parameters at post-treatment follow-up (N=30)

Clinical Parameters	Mean±SD
Hemoglobin	10.02±0.99
Neutrophil	65.50±5.75
Leukocytes	23.07±3.68
Platelet (*10^5)	2.06±0.46

The post-treatment follow-up of clinical parameters for the 30 participants revealed the following mean values with standard deviations (SD): The mean hemoglobin level was 10.02±0.99 g/dL, indicating a slight decrease from the baseline. The mean neutrophil percentage was 65.50±5.75%, showing a marginal increase. The mean leukocyte count was 23.07±3.68 (units unspecified), which remained relatively stable compared to baseline. The mean platelet count was 2.06±0.46 x 10^5/µL, reflecting a slight decrease.

Table 6: Comparison of baseline and post-treatment clinical parameters among the participants (N=30)

Paired Differences	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference		Sig. (2-tailed)
				Lower	Upper	
Hemoglobin - Hemoglobin	0.54828	0.87665	0.16279	0.21481	0.88174	**0.002**
Neutrophil - Neutrophil	-1.5	7.454	1.361	-4.284	1.284	0.279
Leukocytes - Leukocytes	0.4	2.811	0.513	-0.65	1.45	0.442
Platelet (^5) - Platelet (^5)	0.279	0.48879	0.08924	0.09648	0.46152	**0.004**

The comparison of baseline and post-treatment clinical parameters among the 30 participants yielded significant findings. The mean difference in hemoglobin levels from baseline to post-treatment was 0.54828 g/dL with a standard deviation of 0.87665, and a standard error mean of 0.16279. The 95% confidence interval of the difference ranged from 0.21481 to 0.88174, with a significant p-value of 0.002, indicating a statistically significant decrease in hemoglobin levels post-treatment. For neutrophils, the mean difference was -1.5% with a standard deviation of 7.454 and a standard error mean of 1.361. The 95% confidence interval ranged from -4.284 to 1.284, and the p-value was 0.279, suggesting no significant change in neutrophil percentage post-treatment. The mean difference in leukocyte counts was 0.4 (units unspecified) with a standard deviation of 2.811 and a standard error mean of 0.513. The 95% confidence interval ranged from -0.65 to 1.45, with a p-value of 0.442, indicating no significant change in leukocyte counts post-treatment. The platelet count showed a mean difference of 0.279 x 10^5/µL with a standard deviation of 0.48879 and a standard error mean of 0.08924. The 95% confidence interval ranged from 0.09648 to 0.46152, with a significant p-value of 0.004, indicating a statistically significant decrease in platelet counts post-treatment.

IV. Discussion

The present retrospective observational study aimed to evaluate the clinical characteristics, treatment responses, and hematological changes in HER2-positive breast cancer patients undergoing adjuvant trastuzumab therapy. The findings of our study are consistent with previous literature and provide valuable insights into the management and outcomes of this patient cohort. The demographic profile of the 30 HER2-positive breast cancer patients revealed a predominance of women aged 41-50 years (43.33%) and a significant majority with left breast involvement (83.33%). These findings align with global epidemiological data indicating the higher incidence of breast cancer in the fourth and fifth decades of life and the relatively higher occurrence in the left breast (18). Our study's baseline clinical parameters showed mean hemoglobin levels of 11.06±1.03 g/dL, neutrophil percentage of 64.00±9.49%, leukocyte count of 23.47±3.29, and platelet count of 2.34±0.57 x 10^5/µL, which provide a comprehensive hematological profile for this patient group. Similar hematological profiles have been observed in other studies, emphasizing the importance of monitoring these parameters for assessing treatment tolerance and patient safety (19). Tumor characteristics at baseline indicated that 40.00% of patients had T1c tumors, 26.67% had T2 tumors, and 33.33% had T3 tumors, with 86.67% showing positive lymph node metastasis and 43.33% at stage IIIA. These findings emphasize the aggressive nature of HER2-positive breast cancer, as reflected in other studies where larger tumor sizes and higher rates of lymph node involvement are prevalent (20,21). The hormone receptor status at baseline showed that 86.67% of patients were both ER+ and PgR+, indicating a significant proportion of hormone receptor positivity within the HER2-positive cohort, consistent with the findings of Lee et al. (22). Post-treatment evaluations revealed changes in tumor sizes, with a slight increase in T1b cases to 6.67%, while T1c remained at 40.00%, T2 decreased to 20.00%, and T3 stayed at 33.33%. Lymph node metastasis and stage IIIA presence remained consistent at 86.67% and 43.33%, respectively. These results highlight the persistent challenges in achieving complete remission in advanced-stage HER2-positive breast cancer patients, corroborating findings from studies such as those by Curigliano et al. and Gwark et al. (20,21). The hormone receptor status post-treatment indicated a slight increase to 90.00% ER+ and PgR+, reflecting the dynamic nature of tumor biology under therapeutic pressure (23). One of the significant findings of our study was the statistically significant decrease in hemoglobin levels (mean difference of 0.54828 g/dL, p=0.002) and platelet counts (mean difference of 0.279 x 10^5/µL, p=0.004) post-treatment. These hematological changes are consistent with those reported by Raza et al., who observed similar decreases in hemoglobin and RBC counts post-treatment, emphasizing the need for vigilant hematological monitoring during therapy (24). In contrast, neutrophil and leukocyte counts showed no significant changes post-treatment, with mean differences of -1.5% (p=0.279) and 0.4 (p=0.442), respectively. This stability in neutrophil and leukocyte counts is corroborated by findings from Hao et al., indicating that these parameters may not be as adversely affected by trastuzumab therapy as hemoglobin and platelet levels

(25). The high prevalence of combined hormone therapy (86.67%) among the participants underscores the integrated treatment approach for managing HER2-positive breast cancer, which aligns with current therapeutic guidelines and findings from studies such as those by Zattarin et al. and Pernas et al., who highlight the benefits of combining hormonal therapies with anti-HER2 treatments to improve clinical outcomes (26,27). In conclusion, our study provides a detailed overview of the clinical and hematological characteristics of HER2-positive breast cancer patients undergoing trastuzumab therapy. The findings highlight the aggressive nature of the disease, the necessity for comprehensive treatment strategies, and the importance of continuous monitoring of hematological parameters to manage potential side effects effectively. These insights contribute to the growing body of literature on the management of HER2-positive breast cancer and stress the need for ongoing research to optimize treatment protocols and improve patient outcomes.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

V. Conclusion

In conclusion, this retrospective observational study highlights the clinical characteristics, treatment outcomes, and hematological changes in HER2-positive breast cancer patients receiving adjuvant trastuzumab therapy. The findings emphasize the aggressive nature of HER2-positive breast cancer and the significant therapeutic impact of trastuzumab, despite persistent challenges in achieving complete remission and managing side effects. The statistically significant decreases in hemoglobin and platelet levels post-treatment emphasize the need for continuous monitoring and management of hematological parameters. The study also underscores the importance of integrating hormone therapy with trastuzumab to enhance treatment efficacy. These insights contribute to the existing body of knowledge and call attention to the need for ongoing research to optimize treatment protocols and improve patient outcomes in HER2-positive breast cancer.

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