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Adverse effects of Herceptin treatment in women with breast cancer in Hillah (Iraq)

Amal Talib Al Sa'ady[1,*], Lina Alisawi[1], Dhafar Mohamed Hasan Al-Shareefy[1], Nadia H. Kadhum[1], Hamid Khalaf Mutar[2], Ghadeer Talib Khlaif[3]

[1]Department of Clinical Laboratory Sciences, College of Pharmacy, University of Babylon, Hillah, Iraq
[2]Department of English Language and Literature, College of Arts and Human Sciences, Al-Mustaqbal University, Hillah, Iraq
[3]Department of Radiology Techniques, College of Health and Medical Techniques, Al-Mustaqbal University, Hillah, Iraq

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*** CORRESPONDING AUTHOR:**
Amal Talib Al Sa'ady, Department of Clinical Laboratory Sciences, College of Pharmacy, University of Babylon, Hillah, Iraq; e-mail: amal.atiyah@yahoo.com

ABSTRACT

Herceptin (trastuzumab) is a targeted anticancer therapy that has significantly improved outcomes in the treatment of human epidermal growth factor receptor 2 (HER2)-positive breast cancer since its introduction in 1998. This study has employed a retrospective cross-sectional design using a paper-based questionnaire administered to women with breast cancer and receiving Herceptin at the Oncology Center of the Imam Sadiq Teaching Hospital and at the Marjan Medical City Hospital in Hillah, Iraq. The study period spanned from 1 November 2022 to 31 March 2023. A total of 50 Iraqi women aged 21 to 71 years participated in the study. The most common age groups were 41–50 and 51–60 years. Of the participants, 49 (98%) had undergone breast surgery. Seventeen distinct adverse effects associated with Herceptin use were reported, with all patients (100%) experiencing at least one. The most frequently reported effects included fatigue, exhaustion, and loss of energy, bone and muscle pain, headache, anorexia, gastrointestinal pain (cramping), sleep disturbances, visual disturbances, as well as bloating and increased abdominal size. These were followed by drowsiness, prolonged sleep, cardiac issues, anaemia, itching and skin allergies, as well as immunodeficiency. Less common adverse effects included hypertension, hyperglycaemia, kidney problems, and hypercholesterolaemia. Eighteen women (36%) experienced infusion-related reactions, including allergic-like responses and anaphylaxis. Other reported infusion-related reactions included vomiting, severe chills, muscle tremors, high fever, loss of motor control, coughing and choking, shortness of breath, jaw tremors, and temporary loss of speech.

PHARMAKEFTIKI, 37, 2S, 2025 | 135-139

1. Introduction

Patients with HER2-positive breast cancer overexpress the human epidermal growth factor receptor 2 (HER2), which promotes cancer cell proliferation and is associated with a more aggressive disease course compared to other breast cancer subtypes. Herceptin (trastuzumab), a monoclonal antibody, is used as a targeted anticancer therapy. Since its introduction in 1998, Herceptin has significantly improved clinical outcomes in HER2-positive breast cancer. It functions by binding to HER2 on cancer cells, thereby inhibiting its growth-promoting activity[1,2]. Despite its therapeutic benefits, Herceptin is associated with several notable adverse effects. These may include anaphylaxis upon initial administration, dermatological and nail changes, and haematological toxicities (particularly when combined with chemotherapy) which can lead to neutropenia or lymphopenia, thereby increasing susceptibility to infections[3]. Cardiac and pulmonary complications have also been reported[3]. Given the limited data from Iraq on this subject, the present study aimed at documenting the adverse effects of Herceptin treatment in women with breast cancer in a realistic clinical setting.

2. Methodology

This retrospective cross-sectional study employed a paper-based questionnaire targeting women with breast cancer who were receiving Herceptin (as immunotherapy) at the Oncology Centre of Imam Al-Sadiq Teaching Hospital and at the Marjan Medical City Hospital in Hillah, Iraq. The study was conducted from 1 November 2022 to 31 March 2023. The chi-squared test was used in order to assess statistically significant relationships between variables. Participants who provided oral consent were interviewed prior to the administration of their Herceptin dose, with sensitivity to their psychological state. Patients receiving concurrent anticancer therapies alongside Herceptin were excluded in order to minimize confounding effects from overlapping treatment-related side effects. The study received ethical approval from the Ethics Committee of the College of Pharmacy of the University of Babylon (approval number: A-0046; date: 9 February 2025).

3. Results and Discussion

Immunotherapy is among the most promising cancer treatments, developed to enhance the immune system's ability to combat malignancies. Cancer cells often exploit immune regulatory mechanisms in order to suppress immune responses within the tumor microenvironment during disease progression[2,3].

This study included 50 Iraqi women with HER2-positive breast cancer receiving Herceptin, aged between 21 and 71 years. The most common age group was 41–50 years (23 patients; 46%), followed by 51–60 years (18 patients; 36%). Published studies indicate that in developed countries, most women diagnosed with breast cancer are over 63 years old, whereas in developing countries, the majority are under 50 years old[4,5]. Of the participants, 31 (62%) resided in urban areas. Educational attainment varied: 20 (40%) had completed primary education, 10 (20%) had attended middle or high school, 9 (18%) held undergraduate degrees, 3 (6%) had postgraduate qualifications, and 8 (16%) reported other educational backgrounds. Among the 50 women, 49 (98%) had undergone breast surgery: 37 (75.5%) have undergone mastectomy and 12 (24.5%) lumpectomy (Table 1). Most surgeries were performed on women over 40 years of age. Forty patients (80%) began Herceptin treatment postoperatively, while 10 (20%) received it preoperatively (Table 1). A common malpractice in Iraq involves breast cancer surgeries being performed by non-specialist surgeons, contributing to the high prevalence of total mastectomies, which can have profound psychological consequences for patients.

Seventeen distinct adverse effects of Herceptin were recorded, with all patients (100%) experiencing at least one (Table 1). However, a direct comparison of incidence rates with those reported in other studies is not appropriate due to differences in patient populations, study periods, drug manufacturers, and clinical settings. As shown in Table 1, the

PHARMAKEFTIKI, 37, 2S, 2025 | 135-139

Table 1. Adverse effects and infusion reactions associated with Herceptin treatment in the participants of the current study. Notes: *, signifies a statistically significant relationship; **, the total number of women who experienced an infusion reaction was 18 out of 50 (36%).

Variables		Total (%)	Age		Total
			1–40 years	>40 years	
Did you have breast surgery?	yes	49 (98%)	5 (10%)	44 (90%)	50
	no	1 (2%)	0 (0%)	1 (2%)	
Breast surgery	mastectomy	37 (75.5%)	2 (5%)	35 (95%)	49
	lumpectomy	12 (24.5%)	3 (25%)	9 (75%)	
When did you start taking Herceptin?	before surgery	10 (20%)	1 (10%)	9 (90%)	50
	after surgery	40 (80%)	4 (10%)	36 (90%)	
Number of doses given to patients up to the date of the study	1–10 doses	30 (60%)	4 (13%)	26 (87%)	50
	11–20 doses	15 (30%)	3 (20%)	12 (80%)	
	≥21 doses	5 (10%)	0 (0%)	5 (100%)	

Adverse effects associated with Herceptin and their significant relationship with the age

Adverse effects	Total (%)	Age		OR	*p*-value
		1–40 years	>40 years		
Fatigue, exhaustion, and loss of energy	43 (86%)	7	36	2.243	0.01 *
Bone and muscle aches	35 (70%)	2	33	0.005	0.012 *
Headaches	32 (64%)	3	29	1.911	0.011 *
Anorexia	29 (58%)	2	27	0.396	0.022 *
Gastrointestinal pain (cramping)	27 (54%)	5	25	1.189	0.03 *
Sleep disturbances	26 (52%)	2	24	0.015	0.022 *
Visual disturbances	25 (50%)	0	25	0.601	0.031 *
Bloating and increased abdominal size	25 (50%)	0	25	0.807	0.04 *
Drowsiness and prolonged sleep	22 (44%)	0	22	0.165	0.032 *
Heart problems	21 (42%)	3	18	1.624	0.203
Anaemia	14 (28%)	0	14	5.828	0.016 *
Itching and skin allergies	8 (16%)	0	8	3.935	0.047 *
Immunodeficiency	8 (16%)	1	7	0.557	0.809
Hypertension	7 (14%)	1	6	0.092	0.762
Hyperglycaemia	3 (6%)	1	2	0.018	0.893
Kidney problems	3 (6%)	1	2	0.002	0.962
Hypercholesterolaemia	2 (4%)	0	2	0.713	0.398

Infusion reactions **

Reactions during Herceptin infusion	Of N=18 (%)	Reactions during Herceptin infusion	Of N=18 (%)
Vomiting	12 (66.7%)	Loss of motor control	7 (38.9%)
Severe chills	15 (83.4%)	Coughing and choking	7 (38.9%)
Muscle tremors	10 (55.6%)	Loss of consciousness	5 (27.7%)
Fever	12 (66.7%)	Jaw tremors and loss of speech control	3 (16.6%)

most frequently reported side effects included fatigue, exhaustion, and loss of energy, bone and muscle pain, headache, anorexia, gastrointestinal pain (cramping), sleep disturbances, visual disturbances,

PHARMAKEFTIKI, 37, 2S, 2025 | 135-139

as well as bloating and increased abdominal size. These were followed by drowsiness and prolonged sleep, cardiac issues, anaemia, itching and skin allergies, as well as immunodeficiency. Less common effects included hypertension, hyperglycaemia, kidney problems, and hypercholesterolaemia (Table 1). These findings are largely consistent with Herceptin's summary of product characteristics published by Roche.

A statistically significant relationship was observed between patient age and the majority of adverse effects, including fatigue, exhaustion, and loss of energy, musculoskeletal pain, headache, anorexia, gastrointestinal pain (cramping), sleep and visual disturbances, bloating, drowsiness, prolonged sleep, anaemia, itching and skin allergies (Table 1). Patients over 40 years of age were more likely to experience these effects. In contrast, no significant association was found between age and cardiac complications, immunodeficiency, or other less common adverse effects (Table 1).

Cardiomyopathy is a serious adverse effect of Herceptin, particularly when used alone or in combination with paclitaxel following an anthracycline-based chemotherapy. It can range from moderate to life-threatening severity and has led to treatment discontinuation in some patients. For early-stage breast cancer, cardiac function should be assessed at baseline, monitored every three months during treatment, and re-evaluated every 6 months for up to 24 months after treatment cessation[1,2].

Neutropenia is another serious concern, reported more frequently in patients receiving Herceptin in combination with chemotherapy than in those receiving chemotherapy alone. This underscores the importance of vigilant monitoring for signs of infection during Herceptin therapy[6].

Despite Herceptin's clinical success, many of its mechanisms of action and long-term implications remain poorly understood. In severe cases, adverse effects such as congestive heart failure, significant reductions in left ventricular function, severe infusion reactions, and pulmonary toxicity may necessitate the discontinuation of therapy. Additionally, therapeutic resistance to Herceptin has emerged as a major clinical challenge, emphasizing the need for further research into its mechanisms and potential new applications in order to enhance its clinical efficacy[3,7].

Of the 50 participants of our study, 18 (36%) experienced infusion-related reactions, including allergic-like responses and anaphylaxis. Symptoms included vomiting, severe chills, muscle tremors, fever, loss of motor control, coughing and choking, jaw tremors, and loss of speech control (Table 1). Infusion reactions typically occur within minutes to hours during or after administration. Herceptin can cause serious pulmonary toxicity, particularly in patients with pre-existing lung disease or metastatic lung tumours, leading to dyspnoea at rest. Early recognition and immediate clinical intervention are essential so as to ensure patient safety.

The absence of standardized protocols for the prevention, management, and reporting of infusion reactions represents a significant quality and safety gap in oncology care[7,8]. Beyond the medical implications, Herceptin also imposes a substantial economic burden due to its high cost, placing significant strain on national healthcare budgets; particularly in resource-limited countries such as Iraq.

4. Conclusion

Although Herceptin represents a promising and effective treatment for HER2-positive breast cancer, it is associated with a broad spectrum of adverse effects. This survey-based study has documented these effects in a realistic clinical context, thereby contributing to a better understanding of patient experiences and treatment outcomes in Iraq.

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PHARMAKEFTIKI, 37, 2S, 2025 | 135-139

Conflicts of interest

None exist.

ORCIDs

0000-0003-0679-0392 (A.T. Al Sa'ady); 0009-0002-2133-5179 (L. Alisawi); 0009-0007-5534-8628 (D.M.H. Al-Shareefy); 0000-0002-5921-5765 (N.H. Kadhum); 0000-0002-9305-0730 (H.K. Mutar); 0009-0004-3109-5329 (G.T. Khlaif)

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