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## Treatment Patterns and Risk Factors for Breast Cancer in Karbala, Iraq: Findings from a Cross-Sectional Study

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### ABSTRACT

**Background:** Breast cancer is a leading cause of death among Iraqi women, necessitating studies on its demographic and clinical factors to guide diagnosis and treatment approaches. This study aimed to identify the demographic and clinical characteristics of a sample of Iraqi women with breast cancer and predictors of therapy receipt.

**Methods:** A cross-sectional study was conducted in Karbala Province, Iraq, from October 2024 to February 2025 at the Al-Husseini Medical City Oncology Department. Data on age, marital status, employment, residence, menopausal status, family history, disease stage, treatment, and receptor involvement were collected. The  $\chi^2$  test was used to compare the metastatic and nonmetastatic groups. Multinomial logistic regression was used to identify predictors of therapy receipt.

**Results:** Of 1737 recorded cancer cases in Karbala Province, 342 (19.7%) were diagnosed as breast cancer. Among these, 152 cases (44.4%) met the inclusion criteria. Most cases were nonmetastatic ( $n=123$ ; 80.9%), estrogen receptor-positive, progesterone receptor-positive, and underwent surgery and chemotherapy. Family history (odds ratio [OR], 2.75; 95% CI, 1.00–7.54), stage I disease (OR, 4.05; 95% CI, 3.72–4.41), stage II disease (OR, 3.13; 95% CI, 1.91–5.12), stage III disease (OR, 3.56; 95% CI, 2.18–4.66), radiation therapy (OR, 0.02; 95% CI, 0.001–0.55), chemotherapy (OR, 0.15; 95% CI, 0.05–0.50), and targeted therapy (trastuzumab) (OR, 0.03; 95% CI, 0.01–0.18) were associated with hormonal therapy. Being menopausal (OR, 0.08; 95% CI, 0.01–0.60), having human epidermal growth factor receptor 2 (HER2)-positive status (OR, 5.34; 95% CI, 1.51–18.89), and receiving hormonal therapy (OR, 0.02; 95% CI, 0.002–0.18) were associated with targeted therapy (trastuzumab).

**Conclusion:** The findings of this study show that breast cancer treatment decisions—especially for hormonal and targeted therapies—are linked to clinical factors such as hormone receptor status, HER2 involvement, disease stage, and menopausal status.

**Keywords:**

breast neoplasms, risk factors, hormone therapy, molecular targeted therapy

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### INTRODUCTION

Breast cancer is one of the most common types of cancer affecting women worldwide, manifested by the uncontrolled growth of breast cells, and due to its

incidence, mortality, and socioeconomic impact, it represents a major public health concern.<sup>1</sup> Globally, breast cancer accounted for 2.3 million new cases in 2022, resulting in 670 000 deaths in the same year.<sup>2</sup> In Iraq, over 72 000 cases were identified between 2000 and 2019, making it the leading cause of death among Iraqi women, with the highest mortality rate recorded in 2019.<sup>3</sup>

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According to the 2020 Iraqi Cancer Registry, the overall cancer incidence reached approximately 78.9 per 100 000 people, increasing from around 38.9 in 1994.<sup>4</sup> By 2022, the age-standardized incidence had risen to 158.9 per 100 000. Although breast cancer remained a leading diagnosis among women, regional variation was apparent; Karbala's rate was around 111.8 per 100 000.<sup>4</sup> Breast cancer is a multifaceted disease shaped by an array of demographic, genetic, hormonal, and environmental risk factors.<sup>5</sup>

A recent clinical and diagnostic study in Iraq examining the association between breast cancer and periodontal disease suggested potential links between chronic inflammation and tumor progression, underscoring the importance of comprehensive patient evaluation beyond traditional oncological parameters.<sup>6</sup>

At the molecular level, the interplay of genetic mutations and inflammatory mediators also shapes breast cancer pathogenesis and response to treatment. A notable example is the correlation between tumor suppressor protein p53 and inflammatory cytokines such as interleukin 2 (IL-2) and interleukin 8 (IL-8), which have been found to contribute to tumor growth, immune evasion, and metastasis.<sup>7</sup>

Breast cancer therapy typically involves a combination of surgery, radiation, chemotherapy, hormonal agents, and targeted treatments, selected based on the tumor's staging, hormone receptor and human epidermal growth factor receptor 2 (HER2) status, age, and other clinicopathological features.<sup>8</sup>

Given its significance as a leading cause of death among Iraqi women, this study sought to explore the demographic and clinical characteristics of Iraqi women with breast cancer, focusing on identifying potential predictors of treatment receipt. By investigating this underserved population, the study aims to fill gaps in the existing literature and provide insights into factors influencing therapy access and outcomes in this context.

## METHODS

A cross-sectional study was conducted in Karbala province, Iraq, at the Oncology Department in Al-Husseini Medical City from October 2024 to February 2025. The study included women with a confirmed diagnosis of breast cancer via histopathological examination of tissue obtained by core needle biopsy or surgical excision and supported by clinical assessment and imaging techniques such as mammography and ultrasound.

Eligible participants were newly diagnosed or previously treated patients who received care at the oncology department and had complete medical records available. Women diagnosed with other types of cancer, those with incomplete medical records,

individuals who did not receive treatment from the oncology department, or those residing outside Karbala province were excluded.

The study sample was drawn from 1737 cancer cases reported in Karbala province. Among these, 342 cases (19.7%) were diagnosed with breast cancer. After applying the inclusion and exclusion criteria, 152 breast cancer cases (44.4% of breast cancer cases) were included in the final analysis. Although a formal a priori power calculation was not performed, the available sample size was determined by the number of eligible cases within the registry during the study period.

Data were collected from the medical records of the included cases using a Microsoft Excel sheet. Collected data included age, marital status, employment status, residence, and menopausal status. Additionally, each participant's body mass index (BMI) was calculated to determine obesity status, along with family history, breast cancer stage according to the number staging system<sup>9</sup>, metastatic status, type of treatment used, and hormonal receptor involvement.

Data on age, marital status, employment, menopausal status, family history, treatment type, and residence were obtained from patients' medical records. We also obtained data on their weight and height to calculate their BMI to determine obesity status.

Breast cancer stage was determined according to the number staging system<sup>9</sup>, using data from imaging, clinical examination, and pathological reports at the time of diagnosis.

Metastatic status was assessed through imaging (e.g., computed tomography [CT] scan) and recorded from radiology reports.

Hormone receptor involvement and human epidermal growth factor receptor 2 (HER2) expression were assessed using immunohistochemistry (IHC) performed on tumor tissue samples.

The data were analyzed using IBM SPSS Software, version 25. Descriptive statistics were expressed as frequencies and percentages. The  $\chi^2$  test was used to compare the metastatic and nonmetastatic groups, but no correction for multiple comparisons was applied. Multinomial logistic regression analysis was performed to identify factors associated with the type of treatment used.

Because the outcome was a categorical variable with more than 2 nonordinal levels, multinomial logistic regression was the appropriate modeling technique. This method allowed for estimating the likelihood of receiving each treatment type relative to a reference category while simultaneously adjusting for multiple covariates. Adjusted odds ratios (ORs)



with 95% CIs and a P value of  $<0.05$  were used to indicate statistical significance.

The use of a multivariable multinomial logistic regression allowed us to more accurately estimate the independent effect of each factor on the likelihood of receiving hormonal or targeted therapy compared with other therapies. Variables were considered for inclusion in the final multinomial logistic regression model if they showed a P value  $<0.20$  in univariable analysis, were clinically relevant, or were supported by prior literature. This combined approach was used to minimize residual confounding and enhance model validity. Multicollinearity was assessed, and the number of predictors was limited relative to the sample size to avoid overfitting.

## RESULTS

Of 1737 recorded cancer cases in Karbala province, 342 (19.7%) were diagnosed as breast

cancer. Among these, 152 cases (44.4%) met the inclusion criteria and were enrolled in this cross-sectional analysis. The age of the included cases ranged from 24 to 80 years, and the mean (SD) age was 52.15 (12.30) years. The majority of the included cases (n = 123; 80.9%) presented with nonmetastatic disease.

Compared with cases with metastasis, the majority of nonmetastatic cases were older than 40 years (83.7%), unemployed (79.7%), and postmenopausal (69.9%). Most of these patients had no reported family history of breast cancer (65.9%) and were classified as obese (70.7%), indicating a predominance of lifestyle and demographic risk factors among these cases (Table 1). In terms of clinical characteristics and treatment, the nonmetastatic cases were significantly more likely to be estrogen receptor (ER) – positive

**Table 1.** Sociodemographic Characteristics of Study Participants

Variables	Total (N=152)	Nonmetastatic (n=123)	Metastatic (n=29)	P value
Age, y				0.90
≤40	25 (16.4)	20 (16.3)	5 (17.2)	
>40	127 (83.6)	103 (83.7)	24 (82.8)	
Marital status				0.37
Single	6 (3.9)	4 (3.3)	2 (6.9)	
Married	146 (96.1)	119 (96.7)	27 (93.1)	
Employment				0.21
Yes	28 (18.4)	25 (20.3)	3 (10.3)	
No	124 (81.6)	98 (79.7)	26 (89.7)	
Residence				>0.99
Rural	42 (27.6)	34 (27.6)	8 (27.6)	
Urban	110 (72.4)	89 (72.4)	21 (72.4)	
Menopausal status				0.92
Yes	106 (69.7)	86 (69.9)	20 (69.0)	
No	46 (30.3)	37 (30.1)	9 (31.0)	
Contraceptive use				0.54
Yes	60 (39.5)	50 (40.7)	10 (34.5)	
No	92 (60.5)	73 (59.3)	19 (65.5)	
Age at first pregnancy, y				0.81
13–23	86 (56.6)	71 (57.7)	15 (51.7)	
24–43	50 (32.9)	39 (31.7)	11 (37.9)	
No children	16 (10.5)	13 (10.6)	3 (10.3)	
Family history				0.75
Yes	51 (33.6)	42 (34.1)	9 (31.0)	
No	101 (66.4)	81 (65.9)	20 (69.0)	
Obesity				0.85
Yes	107 (70.4)	87 (70.7)	20 (69.0)	
No	45 (29.6)	36 (29.3)	9 (31.0)	

Data are presented as No. (%) unless otherwise indicated.



(88.6%;  $P = 0.008$ ), progesterone receptor (PR)-positive (83.7%;  $P = 0.027$ ), and more likely to receive surgical intervention (91.1%;  $P < 0.001$ ) and chemotherapy (77.2%;  $P < 0.001$ ) (Table 2).

**Table 2.** Clinical Characteristics and Treatment Profile of Study Cases Variables

	Total (N=152)	Nonmetastatic (n=123)	Metastatic (n=29)	P value
Tumor location				0.40
Left breast	68 (44.7)	58 (47.2)	10 (34.5)	
Right breast	73 (48.0)	56 (45.5)	17 (58.6)	
Both	11 (7.2)	9 (7.3)	2 (6.9)	
Breast cancer stage				<0.001 <sup>a</sup>
I	15 (9.9)	15 (12.2)	0	
II	50 (32.9)	50 (40.7)	0	
III	57 (37.5)	57 (46.3)	0	
IV	30 (19.7)	1 (0.8)	29 (100.0)	
ER status				0.008 <sup>a</sup>
Positive	129 (84.9)	109 (88.6)	20 (69.0)	
Negative	23 (15.1)	14 (11.4)	9 (31.0)	
PR status				0.03 <sup>a</sup>
Positive	122 (80.3)	103 (83.7)	19 (65.5)	
Negative	30 (19.7)	20 (16.3)	10 (34.5)	
HER2 status				0.13
Positive	50 (32.9)	37 (30.1)	13 (44.8)	
Negative	102 (67.1)	86 (69.9)	16 (55.2)	
Surgery				<0.001 <sup>a</sup>
Yes	116 (76.3)	112 (91.1)	4 (13.8)	
No	36 (23.7)	11 (8.9)	25 (86.2)	
Radiation therapy				0.32
Yes	12 (7.9)	11 (8.9)	1 (3.4)	
No	140 (92.1)	112 (91.1)	28 (96.6)	
Chemotherapy				<0.001 <sup>a</sup>
Yes	104 (68.4)	95 (77.2)	9 (31.0)	
No	48 (31.6)	28 (22.8)	20 (69.0)	
Hormonal therapy				0.61
Yes	64 (42.1)	53 (43.1)	11 (37.9)	
No	88 (57.9)	70 (56.9)	18 (62.1)	
Targeted therapy (trastuzumab)				0.27
Yes	40 (26.3)	30 (24.4)	10 (34.5)	
No	112 (73.7)	93 (75.6)	19 (65.5)	

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PR, progesterone receptor.

Data are presented as No. (%). <sup>a</sup>Statistically significant.



Multinomial logistic regression analysis identified several factors significantly associated with the likelihood of receiving hormonal therapy. Patients with a family history of breast cancer were more likely to receive hormonal treatment (OR, 2.75; 95% CI, 1.00–7.54;  $P=0.049$ ), suggesting a clinical tendency to prescribe endocrine therapy in genetically predisposed individuals. Disease stage was also a strong predictor. Stage I had 4-fold higher odds of receiving hormonal therapy (OR, 4.05; 95% CI, 3.72–4.41;  $P<0.001$ ), stage II had more than 3-fold increased odds (OR, 3.13; 95% CI, 1.91–5.12;  $P<0.001$ ), and stage III showed a similar significant

association (OR, 3.56; 95% CI, 2.18–4.66;  $P<0.001$ ). Those who received radiation therapy were also significantly more likely to be on hormonal therapy, although the OR was notably low (OR, 0.02; 95% CI, 0.001–0.55;  $P=0.02$ ). Similarly, chemotherapy (OR, 0.15; 95% CI, 0.05–0.50;  $P=0.002$ ) and targeted therapy (trastuzumab) (OR, 0.03; 95% CI, 0.01–0.18;  $P<0.001$ ) were significantly associated with hormonal therapy. These associations reflect the frequent use of hormonal therapy as part of combined systemic treatment regimens (Table 3).

**Table 3.** Factors Associated with Hormonal Therapy vs Other Treatment Modalities Identified by Multinomial Logistic Regression

Variables	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Age ≤40 y	5.61 (0.72–43.52)	0.10	0.30 (0.04–2.25)	0.26
Marital status (married)	0.72 (0.04–12.81)	0.83	1.45 (0.08–25.81)	0.80
Employment (yes)	0.62 (0.18–2.14)	0.45	1.63 (0.46–5.78)	0.45
Residence (rural)	1.91 (0.71–5.13)	0.20	0.64 (0.23–1.77)	0.39
Menopausal status (yes)	3.80 (0.75–19.40)	0.11	0.26 (0.05–1.36)	0.11
Obesity (yes)	0.59 (0.22–1.64)	0.31	1.56 (0.55–4.43)	0.41
Contraceptive use (yes)	0.84 (0.31–2.24)	0.72	1.20 (0.44–3.27)	0.73
Family history (yes)	0.42 (0.16–1.11)	0.08	2.75 (1.00–7.54)	0.049
Age at first pregnancy, y				
13–23	2.80 (0.44–17.65)	0.27	0.30 (0.05–1.94)	0.20
24–43	2.78 (0.40–19.36)	0.30	0.33 (0.05–2.39)	0.27
Tumor location				
Left breast	0.29 (0.04–2.29)	0.24	4.70 (0.52–42.28)	0.17
Right breast	0.61 (0.08–4.57)	0.63	1.72 (0.21–14.06)	0.61
Breast cancer stage				
Stage I	0.99 (0.11–8.67)	0.99	4.05 (3.72–4.41)	<0.001
Stage II	1.13 (0.22–5.94)	0.86	3.13 (1.91–5.12)	<0.001
Stage III	1.13 (0.18–7.11)	0.90	3.56 (2.18–4.66)	<0.001
ER status (positive)	0.46 (0.03–6.59)	0.56	3.57 (0.23–55.06)	0.36
PR status (positive)	2.67 (0.28–26.02)	0.40	0.25 (0.02–2.65)	0.25
HER2 status (positive)	2.24 (0.73–6.93)	0.16	0.45 (0.14–1.44)	0.18
Surgery	0.62 (0.14–2.74)	0.52	0.87 (0.17–4.29)	0.86
Radiation therapy	5.82 (0.58–57.97)	0.13	0.02 (0.001–0.55)	0.02
Chemotherapy	4.49 (1.52–13.25)	0.007	0.15 (0.05–0.50)	0.002
Targeted therapy (trastuzumab)	33.58 (5.47–206.12)	<0.001	0.03 (0.01–0.18)	<0.001

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; OR, odds ratio; PR, progesterone receptor. Reference category: other therapy.

Menopausal status was significantly associated with a lower likelihood of receiving targeted therapy. Postmenopausal women had reduced odds compared with premenopausal women (OR, 0.08; 95% CI, 0.01–0.60;  $P=0.01$ ), suggesting that younger, premenopausal patients were more likely to receive HER2-targeted treatment. HER2 positivity was a strong independent predictor of targeted therapy administration, with HER2-positive patients having more than 5-fold greater odds of receiving trastuzumab compared with HER2-negative counterparts (OR, 5.34; 95% CI, 1.51–18.89;  $P=0.009$ ).

In addition, the use of hormonal therapy was significantly associated with targeted therapy (OR, 0.02; 95% CI, 0.002–0.18;  $P<0.001$ ), indicating a substantial overlap in treatment modalities among hormone receptor-positive, HER2-positive patients (Table 4).

## DISCUSSION

This study analyzed the patterns of breast cancer treatment in Karbala, Iraq, and identified several demographic, clinical, and pathological factors significantly associated with the use of hormonal and targeted therapies. The findings underscore not only



biological determinants such as receptor status but also systemic and demographic influences that shape treatment decisions in the Iraqi healthcare context. Karbala's breast cancer proportion aligns closely with both national and regional data. On the national level,

breast cancer constituted 19.5% of all new cancers and 34% of female cancers, with an incidence of nearly 22 per 100 000 women. Similar figures are reported from regional registries, confirming breast cancer as the most common malignancy in women.<sup>10</sup>

**Table 4.** Factors Associated With Targeted Therapy vs Other Treatment Modalities Identified by Multinomial Logistic Regression

Variables	Univariable		Multivariable	
	OR (95% CI)	P value	OR (95% CI)	P value
Age ≤40 y	4.54 (0.52–39.54)	0.17	0.17 (0.02–1.37)	0.10
Marital status (married)	1.87 (0.01–313.71)	0.81	0.68 (0.01–91.25)	0.88
Employment (yes)	0.36 (0.08–1.69)	0.20	3.02 (0.64–14.28)	0.16
Residence (rural)	2.08 (0.55–7.85)	0.28	0.40 (0.11–1.41)	0.15
Menopausal status (yes)	11.35 (1.52–84.67)	0.02	0.08 (0.01–0.60)	0.01
Obesity (yes)	0.63 (0.17–2.40)	0.50	1.64 (0.44–6.09)	0.46
Contraceptive use (yes)	1.17 (0.35–4.00)	0.80	0.83 (0.26–2.68)	0.75
Family history (yes)	0.77 (0.21–2.78)	0.69	1.30 (0.37–4.53)	0.68
Age at first pregnancy, y				
13–23	0.65 (0.01–56.49)	0.85	1.10 (0.02–74.78)	0.96
24–43	0.45 (0.01–40.31)	0.73	1.53 (0.02–104.97)	0.84
Tumor location				
Left breast	4.25 (0.48–37.72)	0.19	0.25 (0.03–2.04)	0.20
Right breast	4.00 (0.49–32.75)	0.20	0.26 (0.03–2.01)	0.20
Metastatic (yes)	1.39 (0.13–14.40)	0.27	0.72 (0.07–7.44)	0.78
ER status (positive)	1.61 (0.12–21.04)	0.72	0.39 (0.04–4.08)	0.43
PR status (positive)	2.52 (0.25–25.23)	0.43	0.54 (0.07–4.29)	0.56
HER2 status (positive)	0.18 (0.05–0.66)	0.009	5.34 (1.51–18.89)	0.009
Surgery	1.40 (0.16–11.90)	0.76	0.81 (0.11–6.33)	0.84
Radiation therapy	0.63 (0.09–4.45)	0.65	1.50 (0.21–10.96)	0.69
Chemotherapy	1.75 (0.29–10.62)	0.54	0.64 (0.11–3.57)	0.61
Hormonal therapy	39.21 (4.94–311.19)	0.001	0.02 (0.002–0.18)	<0.001

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; OR, odds ratio; PR, progesterone receptor.

Reference category: other therapy.

The predominance of nonmetastatic, hormone receptor-positive cases aligns with regional and global trends, where ER-positive/PR-positive tumors account for a significant proportion of early-stage breast cancer. The involvement of ER and PR receptors in the early stages of breast cancer can be a good prognostic indicator, which can result in slow disease progression and improved survival rates.<sup>11</sup> ER/PR positivity (approximately 81%) is higher than national averages, in which ER positivity ranged around 66% to 68%, PR around 64% to 65%, and HER2 around 29% to 49%.<sup>12,13</sup> In the Middle East region, analyses report luminal A and triple-positive subtypes, accounting for approximately 55% to 60% of cases.<sup>12</sup> Recent studies demonstrate that while ER-positive/PR-positive tumors exhibit favorable responses to endocrine therapy and improved survival, ER-positive/PR-negative cancers are associated with more aggressive features, poorer treatment response, and higher risk of distant recurrence, underscoring the prognostic value of combined hormone receptor profiling.<sup>14,15</sup>

The current study found that patients with nonmetastatic (80.9%) breast cancer were more likely

to undergo surgery (91.1%) and receive chemotherapy (77.2%), reflecting adherence to international guidelines for localized disease. Similarly, a study by Namiq *et al.* reported that in Iraq, nonmetastatic cases typically undergo surgery, with mastectomy being more common, although breast-conserving surgery is increasingly practiced.<sup>16</sup> This contrasts with the report by Abood *et al.* of 49% of cases presenting as locally advanced or metastatic.<sup>17</sup>

The study found that hormonal therapy was more commonly administered to patients with early-stage breast cancer, suggesting that early diagnosis remains crucial for the optimal use of endocrine treatments. In Najaf province in Iraq, between 2019 and 2021, hormonal therapy was significantly more common among early-stage and ER<sup>+</sup>/PR<sup>+</sup> cases.<sup>18</sup> Similarly, in Baghdad, the capital of Iraq, hormonal therapy uptake was high among patients with stage I and II disease with receptor positivity.<sup>12</sup>

The study also showed that those who received hormonal therapy had a family history of breast cancer. This could reflect physician perceptions of higher recurrence risk or better adherence among



genetically predisposed individuals. However, it also raises the question of whether genetic counseling and testing services are sufficiently available or standardized in Iraq. Regional variations exist in Iraq regarding the association between hormonal therapy and family history of breast cancer. In Najaf, only 22.7% of 251 patients had a positive family history, with many being hormone receptor-negative.<sup>18</sup> Conversely, in Baghdad, 68.1% of 100 women receiving hormonal therapy reported a family history, demonstrating a strong correlation between familial risk and hormone receptor-positive (ER<sup>+</sup>/HER2<sup>+</sup>) status.<sup>19</sup> These disparities suggest geographical differences in both genetic predisposition and treatment patterns.

One particularly notable and counterintuitive finding was the strong inverse association between receiving radiation therapy and hormonal treatment. This finding contradicts those from national studies. A cross-sectional study of Iraqi patients treated with adjuvant 3-dimensional conformal radiotherapy (3D-CRT) reported that radiation was commonly administered to luminal subtypes, which are ER<sup>+</sup>/PR<sup>+</sup> tumors that also receive hormonal therapy.<sup>20</sup> Another study by Al-Alwan *et al.* found that approximately 34.2% of ER<sup>+</sup>/PR<sup>+</sup> breast cancer patients responded to tamoxifen, with hormonal therapy often used alongside radiation as part of multimodality treatment.<sup>21</sup> This discrepancy suggests that the snapshot nature of the cross-sectional design may not fully capture the standard sequence of multimodal treatment.

The study found that both menopausal status and HER2 positivity are significant predictors of receiving targeted therapy in women with breast cancer. Trastuzumab remains the cornerstone of treatment for HER2-overexpressing tumors.<sup>22</sup> However, the relatively low use of targeted therapy compared with global data may reflect limited access to biologic agents due to cost, insurance coverage, or drug availability in the public healthcare sector.<sup>23,24</sup> The evidence from national studies shows no significant statistical association between HER2-positive breast cancer and being menopausal among patients eligible for targeted therapy. Although HER2 positivity was common in Iraqi cohorts (approximately 29%–49%), menopausal status was not significantly different in HER2-positive or triple-positive patients.<sup>25</sup> Only the Kurdistan study explicitly tracks the use of targeted therapy, but it does not stratify outcomes by menopausal status.<sup>16</sup> This may reflect age-related disparities in healthcare access or treatment prioritization, which are important to explore further in low- and middle-income countries like Iraq.

This finding highlights the effect of combined hormonal and chemotherapy with targeted therapy on menopausal status. In real-world Iraqi practice, combination therapy (chemotherapy, targeted HER2 therapy, endocrine therapy) is dictated by tumor biology—hormone receptor/HER2 status—not menopausal status.<sup>16</sup> A randomized controlled trial by Francis *et al.* has shown that the combination of ovarian suppression with tamoxifen or exemestane results in a reduction of recurrence in premenopausal women with breast cancer, especially in hormone-positive women, in whom ovarian suppression induces menopause, facilitating treatment effectiveness.<sup>26</sup> Furthermore, Del Mastro *et al.* found that combined chemotherapy and HER2-targeted therapy in the long term may result in early ovarian failure, which is not directly related to targeted therapies like trastuzumab but to the risk of chemotherapy-induced menopause.<sup>27</sup>

The study also showed that those who received targeted therapy also received hormonal therapy. The significant overlap between hormonal and targeted therapies reinforces the growing shift toward personalized treatment strategies in breast cancer management. This is particularly important in settings with constrained resources, where understanding which patients benefit most from dual-modality treatment could improve outcomes and resource allocation. The data from Iraqi studies support our findings. When breast cancer is HER2<sup>+</sup> and hormone receptor-positive (ER<sup>+</sup>/PR<sup>+</sup>), patients commonly receive both hormonal and targeted therapy. However, these studies often do not explicitly quantify how many patients received both therapies unless they are triple-positive.<sup>16,28,29</sup> This combination consistently yields better survival, delayed progression, and improved quality of life.<sup>30–32</sup>

Although the study covered several aspects of breast cancer, some limitations are important to mention. The relatively small sample size may limit the generalizability of the findings. Because the study was cross-sectional, causality cannot be firmly established. Additional limitations included incomplete medical records, which restricted our analysis of molecular subtypes beyond ER/PR/HER2 status and prevented evaluation of socioeconomic factors, comorbidities, and patient preferences. Furthermore, by including only cases with complete records from a single center in Kerbala, our study may be subject to selection bias. Additionally, because the data were drawn from a single province, they may not fully capture the variability in healthcare infrastructure, diagnostic capacity, or treatment access across Iraq. Future multicenter or population-based studies would help validate the generalizability of these findings.



Although medical records served as the primary data source, variability in documentation quality, inconsistent data entry, and potential missing values may have influenced the accuracy and completeness of some clinical variables. To mitigate these issues, strict inclusion criteria were applied; however, this may itself introduce selection bias by excluding patients whose records were incomplete or managed outside the primary study center.

The results highlight the urgent need to strengthen early detection programs, improve access to HER2-targeted therapies, and enhance molecular diagnostics in Iraq. Access to targeted therapies should be prioritized through national policy, subsidized procurement, and biosimilar adoption. Investment in oncology infrastructure, public health education, and clinical training is essential to optimize breast cancer outcomes in line with international standards. Moreover, efforts to integrate genetic risk assessment and survivorship planning into routine care could further personalize treatment and follow-up.

## CONCLUSION

This study shows that breast cancer accounts for a significant proportion of all cancer cases in Karbala province, Iraq. Among the eligible cases, the majority were nonmetastatic, hormone receptor-positive (ER<sup>+</sup>/PR<sup>+</sup>), and received surgery and chemotherapy as primary treatments. Hormonal therapy use was associated with early-stage disease, family history, radiation, chemotherapy, and targeted therapy. On the other hand, HER2-positive status, menopausal status, and hormonal therapy were all associated with targeted therapy.

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## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

## ETHICAL CONSIDERATIONS

The study received ethical approval from the scientific and ethical committee of the College of Pharmacy, University of Kerbala (Project No. 2025HU3).

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## DATA AVAILABILITY

No new data were created or analyzed in this study. Data sharing is not applicable to this article.

## AI DISCLOSURE

Artificial intelligence tools, including Perplexity AI No generative AI tools were used in the design, analysis, or writing of this manuscript.

## AUTHOR CONTRIBUTIONS

LM contributed to the study design and implementation, analysis of the study results, and writing of the manuscript. MR contributed to the review and editing of the manuscript and supervised the study. IN assisted in data collection, provided critical feedback, and supported the research, analysis, and manuscript.



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