Editorial Process: Submission:11/07/2024 Acceptance:04/14/2025

Survival Values of Iraqi Male Breast Cancer

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Abstract

Background: Male breast cancer (mBC) is a rare disease, accounting for approximately 1% of all breast cancers. In Iraq, the mBC rate was 0.39% for all cancer types by 2022. This study aimed to estimate the survival rates and features of mBC in Iraq. Methods: This was a retrospective survival study. Males with BC were treated between March 2020 and March 2024 at the Department of Radiation Oncology and Department of Medical Oncology. The following data were collected from the records: age, marital status, family history, body mass index, surgery type, chemotherapy, radiotherapy, hormonal therapy, recurrence and/or metastasis, period of follow-up, histological type, tumor size, tumor grade, tumor stage, estrogen and/or progesterone receptor expression, HER2 neu status, metastasis site, BC side, and lymph node positivity. **Results:** The mean age of the patients was (54.75 ± 12.25) . The majority (95.7%) of the patients were married, and only (17.4%) of patients presented with a positive family history. Most patients underwent surgery (21, 91.3%), chemotherapy (19, 86.4%), radiotherapy (13, 59.1%), and hormonal therapy (15, 68.2%). The mean follow-up was (30.73 ± 24.55) months. The majority (16, 88.9%) of the patients presented with positive PR and ER, and most (11, 64.7%) presented with negative HER-2. The lungs, bones, surgical beds, and multiple sites represented metastasis. Conclusion: The mean age of Iraqi male breast cancer patients was in the upper middle age. Most patients presented with T2 N0 stage, ER/PR positivity, and Her2neu negative. Grade II right invasive ductal carcinoma was reported in half of the men. The median follow-up period was 30 months. Disease free survival (DFS) after full treatment was 75 months.

Keywords: Male breast cancer- HER-2neu- mastectomy- radiotherapy- survival values

Asian Pac J Cancer Prev, 26 (4), 1379-1384

Introduction

Male breast cancer (mBC) is a rare disease, accounting for approximately 1% of breast cancer [1]. Usually, mBC is detected at an advanced stage [2]. Most mBCs are hormone receptor-positive invasive ductal carcinomas, not otherwise specified (IDC NOS) [2]. The risk of mBC increases with age similar to females, yet, men are diagnosed on an average a decade later than women, with a peak around 70 years compared to women [3, 4]. Conclusive evidence suggests that hormone receptor positivity for both ER and PGR is proportionally higher in mBCs (75–90%) than in FBCs [5-7]. Although positivity is an established prognostic factor and therapeutic target for FBC, its role in mBC is not yet well defined because of differences in the scoring systems and cutoff values used, showing high variability in HER-2-positive mBC. Data from retrospective registry studies showed *HER-2* positivity ranging from 1.7% to 56% in the NBC population [8]. Updated studies using standardized HER-2 assessment methods indicated *HER-2* expression in mBC of up to 15% vs. 25%–30% in FBC. Triple-negative tumors in men are extremely rare, and little evidence suggests that prognostic features established in FBC, such as grading and the Ki-67 labeling index, can be applied to NBC. Treatments for mBC have been extrapolated from data on their use in FBC, but limited information is available on the safety and effectiveness of these treatments in men [8, 9].

Similar to breast cancers in women, many of the postulated risk factors for breast cancer in men suggest the importance of anthropometric and hormonal factors. Notably, there is a consistent relationship between obesity and breast cancer in men [10, 11]. Obesity is also linked to an increased risk of breast cancer in postmenopausal women [12]. Studies on mBC concerning hormonally related medical conditions have shown strong associations with Klinefelter syndrome [13].

Several genetic disorders (e.g., Kleinefelter's syndrome) can increase the risk of the disease 50-fold [14].

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A family history of breast and ovarian cancer is reported in approximately 15–20% of men with BC, conferring a relative risk of 2.5 [15]. Moreover, 10% of men with BC have a BRCA2 mutation, and fewer have a BRCA1 mutation [16].

Therefore, the American Society of Clinical Oncology (ASCO) therefore recommends that all men with BC should be offered genetic counseling and testing, regardless of family history [17]. Other genes reported to be mutated in male BC patients are PTEN, p53, and CHEK2. Additional risk factors include obesity, testicular abnormalities, pituitary adenomas that lead to hormonal imbalance, gynecomastia, cirrhosis, exogenous estrogens in men (treated for prostate cancer or transsexuals taking estrogens), race (black men have increased incidence), and radiation exposure [18]. Familial relative risks have been approximately equal between male breast cancer patients with a female family history and females, but data on male-male risks are lacking [19, 20].

The management of male BC is mainly extrapolated from knowledge of female BC [18]. Currently, the most common surgical management is a modified radical mastectomy, whereas breast-conserving treatment (lumpectomy plus radiation therapy) is carried out in no more than one in seven patients [21].

For chemotherapy and radiation therapy, similar indications and regimens were used for female BC. Tamoxifen is the adjuvant endocrine treatment of choice and is recommended for hormone receptor-positive tumors for at least five years [18, 22]. However, the use of aromatase inhibitors in adjuvant settings has been discouraged. The Advanced Breast Cancer (ABC) International Consensus Guidelines state that in metastatic male BC patients who need treatment with an aromatase inhibitor, a concomitant LHRH agonist or orchiectomy is preferred [23-25].

The study aimed to estimate the survival values and features of mBC in Iraq.

Materials and Methods

Study design and setting

This was a retrospective survival study. Males with BC were treated from March 2020 to March 2024 at the Department of Radiation Oncology, Oncology Teaching Hospital, Ministry of Health and Department of Medical Oncology, Baghdad Oncology Teaching Hospital, Baghdad Medical City Complex.

Participants

Inclusion criteria

All males with BC were histopathologically proven.

Exclusion criteria

- 1. Metastatic cases.
- 2. Other primary.
- 3. Unwell or uncomfortable to be enrolled in the study.
- 4. Loss of follow-up cases.

Data collection

The following data were collected from the records:

age, marital status, family history, body mass index, surgery type, chemotherapy, radiotherapy, hormonal therapy, recurrence and/or metastasis, period of followup, histological type, tumor size, tumor grade, tumor stage, estrogen and/or progesterone receptor expression, *HER2* neu status, metastasis site, BC side, and lymph node positivity.

Statistical analysis

SPSS 24.0 (IBM, NY, USA) software package was used for statistical analysis. Calculations of mean values and SD to describe the ordinal data, frequency, and percentage to describe nominal data. Kaplan–Meier analysis was used to estimate survival functions such as DFS. Statistical significance was set at p <0.05. Patients with missing data were excluded from the analysis.

Results

The mean age of the patients was (54.75 ± 12.25) with a minimum age of 33 years and a maximum age of 80 years. The majority (22, 95.7%) of the patients were married, and only (4, 17.4%) of the patients presented with a positive family history. The mean BSA was 1.92 ± 0.204 (range=1.65-2.32) m2. Most patients underwent surgery (21, 91.3%), chemotherapy (19, 86.4%), radiotherapy (13, 59.1%), and hormonal therapy (15, 68.2%). The mean follow-up was (30.73 ± 24.55) months. The majority (16, 88.9%) of the patients presented with positive PR and ER, and most (11, 64.7%) presented with negative *HER-2*. The type of surgery in the majority (19, 82.7%) of patients was MRM+AD, and the majority (16, 66.7%) of patients presented with right breast involvement. The majority (n = 6, 35.3%) of patients presented with (15-20)lymph nodes removed by surgery, and the majority (n = 8,47.1%) of patients presented with (negative lymph nodes) that were removed by surgery. The majority (9, 47.4%) of patients presented with (T2), the majority (7, 36.8%) of patients presented with N1, and only (4, 13.6%) of men had metastasis.

The distribution of patients according to histopathology of male breast cancer including (carcinoma in situ, invasive ductal carcinoma, invasive lobular carcinoma, mixed (IDC and ILC), and medullary carcinoma). Most patients (20, 87.0%) presented with invasive ductal carcinoma.

The distribution of patients according to the grade of male breast cancer including (grade I, II, III, and undifferentiated). The majority (12, 52.2%) of patients presented with grade II disease. The distribution of men according to breast cancer including (stage 0, stage I, stage II, stage III, and stage IV). The majority (9, 39.1%) of patients presented with stages II and III. Pulmonary, bone, surgical bed, and multiple sites represented metastases (Table 1).

Survival rates of men with breast cancer who underwent surgery, chemotherapy, hormonal therapy, and radiotherapy (Figures 1 (a, b, c, and d)).

Discussion

According to our results, the mean age of Iraqi male

Variables		Mean \pm SD/ No.	Range / %
Age (years)		54.75 ±12.25	33-80
Marital status	Married	22	95.7
	Widow	1	4.3
Variables Age (years) Marital status Family history BSA (m ²) Surgery Chemotherapy Radiotherapy Hormonal therapy Period of follow-up (mod PR ER <i>HER2</i> neu Type of surgery Laterality LN	Yes	4	17.4
	No	19	82.6
$BSA(m^2)$		1.92 ± 0.204	1.65-2.32
Surgery	Yes	21	91.3
	No	2	8.7
Chemotherapy	Yes	19	86.4
	No	3	13.6
Radiotherapy	Yes	13	59.1
	No	9	40.9
Hormonal therapy	Yes	15	68.2
	No	7	31.8
Period of follow-up (mor	nths)	30.73 ± 24.55	Mar-81
PR	Positive	16	88.9
	Negative	2	11.1
ER	Positive	16	88.9
	Negative	2	11.1
HER2neu	Positive	4	23.5
	Equivocal	2	11.8
	Negative	11	64.7
Type of surgery	MRM+AD	19	82.7
51 6 5	Ouadrectomy	1	4.3
	Other	3	13
Laterality	Right	16	66.7
5	Left	8	33.3
LN	<5	2	11.8
	5-10	3	17.6
	110-15	4	23.5
	15-20	6	35.3
Laterality LN LN positive	>20	2	11.8
LN positive	0	8	47.1
Marital status Family history Family history BSA (m ²) Surgery Chemotherapy Chemotherapy Radiotherapy Hormonal therapy Period of follow-up (mod PR ER HER2neu Type of surgery Laterality LN IN	1-2	4	23.5
	3-4	2	11.8
	5-6	2	11.8
	>6	- 1	5.9
Т	ТО	3	15.8
1	т 1	1	5.2
	Т 2	9	47.4
	Т 3	2	10.5
Ν	т 4	4	21.1
	N 0	2	10.5
	N 1	- 7	36.8
	N 2	6	31.6
	N 3	۵ ۵	21.1
М	Yes	4	17.4
	No	19	82.6

Table 1. Male and Breast Cancer Characters in This Study

Variables		Mean \pm SD/ No.	Range / %
Site of metastasis	Lung	1	25
	Operative bed	1	25
	Bone	1	25
	Multiple sites	1	25
Histopathology	Carcinoma in situ	2	8.7
	Invasive ductal carcinoma	20	87
	Invasive lobular carcinoma	0	0
	Mixed	1	4.3
	Medullary carcinoma	0	0
Grade	Ι	1	4.3
	II	12	52.2
	III	10	43.5
	IV	0	0
Stage	Ι	1	4.3
	II	9	39.1
	III	9	39.1
	IV	4	17.4

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breast cancer patients is 54 ± 12 years, which is lower than that reported by Lautrup et al. [24], 70 years for males and 61 years for females, and according to Cardoso et al. [22] the mean age of male breast cancer patients is 64 years.

Our study showed that 17.4% of male breast cancer

patients had a family history of breast cancer, which is slightly higher than the 16.2% reported by Zheng et al. (familial associations of male breast cancer with other cancers) [26]. The main histopathological type was invasive ductal carcinoma (87%), in comparison with



Figure 1. a, Survival Kaplen-Meier curve for mBC regarding surgery; b, Survival Kaplen-Meier curve regarding chemotherapy; c, Survival Kaplen-Meier curve regarding hormonal therapy; d, Survival Kaplen-Meier curve after radiotherapy treatment.

with [27, 28].

The main histopathological grade was grade II (52.6%) and grade III (42.1%) in comparison with Salvatore Piscuoglio et al., who found grade II (49%) and grade III (44%) [25]. The hormonal status of Iraqi male breast cancer is lower than the international data as follows: ER±PR positive is 88.2% and Her2 negative is 35.3%, while in comparison with Masci et al. [27], ER±PR positivity was 96.7% and Her2 positive was 16% while in Cardoso et al., ER positivity was 99.3% and Her2 positive was 8.7%. Stage IV at presentation was 19%, which is a very high percentage compared to Cardoso et al. (3.8%) [22].

The site of metastasis cannot be assessed accurately because of the low number of patients with metastasis (4 patients with different sites of metastasis). MRM was the main surgery at 82.7%, which is less than that reported by Giovannamasci et al 91% and this can be explained by the advanced stage of presentation. A large international study, including data from Denmark, reported better survival for MBCP patients than for female breast cancer patients (FBCP) after adjusting for age at diagnosis, stage, and treatment. This suggests that male sex is a favorable prognostic factor. The study lacked complete data about treatment and indication for treatment, prohibiting the conclusion that better treatment of men could improve prognosis [28].

Hormonal status after metastasis was almost comparable to metastasis-naïve, with 88.9% being ERpositive. The disease-free survival (DFS) for male breast cancer was 69 months for all subtypes, but for sub-group analysis, we found that the male who underwent surgery had 76 months DFS while 31 months with no surgery, and this survival is very low in comparison to Cardoso et al., who found that Among M0 patients, median RFS by nodal status was 8.6 years (95% CI, 7.4–11.2) for N0 and 6.4 years [23, 24].

The DFS of male breast cancer patients who received chemotherapy treatment was 72.7 months received chemotherapy while 13 months for those who did not receive chemotherapy, and this was a very low survival outcome. For those who received hormonal therapy, DFS was 75.8% and for hormone-negative patients at 40 months. In Cardoso et al 6.4 the DFS for hormonepositive patients and the very low number of ER-negative tumors, the association of ER with outcome could not be assessed [23, 24].

In conclusions, the mean age of male breast cancer patients in Iraqi is in the upper middle age. Most patients presented with T2 N0 stage, ER/PR positivity, and Her2neu negative. Grade II right invasive ductal carcinoma was reported in half of the men. The median follow-up period was 30 months. DFS after full treatment was 75 months.

Author Contribution Statement

Manwar Al-Naqqash; Conceptualization; Data Curation; Investigation; Methodology; Project administration; Resources; Software; Writing – original draft and Writing – review & editing. Yaala Al-Bairmany; Conceptualization; Data Curation; Investigation; Methodology; Project administration; Resources; Writing – original draft and Writing – review & editing. Waleed Al-Serarati; Conceptualization; Data Curation; Investigation; Methodology; Project administration; Resources; Writing – original draft and Writing – review & editing. Ahmed Alshewered; Conceptualization; Data Curation; Investigation; Methodology; Project administration; Resources; Software; Visualization; Writing – original draft and Writing – review & editing

Acknowledgements

Ethical approval

The Medical Ethical Committee of The Department of Medical Oncology, Baghdad Oncology Teaching Hospital, Baghdad Medical City Complex approved this study (no.015 on 12/2/2020). Participant consent was waived by the committee since only patient files were reviewed.

Conflicts of interest

The authors declare no conflict of interest regarding this article.

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