Original Article

Influence of Educational Background in Pathological Stage and Treatment Modalities in Iranian Breast Cancer Patients: A Retrospective Single-Center Study

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Abstract

Background: Breast cancer (BC) is the most frequently diagnosed visceral cancer, with 13,400 new cases annually in Iranian women. A few studies in Western countries have indicated that BC patients with higher educational backgrounds have a better prognosis than patients with lower educational backgrounds. In a retrospective single-center study, we examined educational background and its relationship with pathological stage and treatment modalities in 3010 BC patients. **Materials and Methods:** The medical records of the patients from the database at the Cancer Research Center of the Shahid Beheshti University of Medical Sciences were reviewed. Univariate logistic regression analysis was used to link educational background to pathological BC stage and treatment modalities. **Results:** The average age at diagnosis was 49.1 ± 11.6 years. Regarding education level, 4.2% of the patients were illiterate, 7.8% had primary school level education, 7.5% had middle school level education, 21.8% had secondary school and diploma level education, 18.6% had university level education and higher, and 40.1% had unspecified level education. Based on the univariate logistic regression analysis, the illiterate group had 65.1% of early-stage BC (Stages I and II) and the university level education and higher group had 73.4% of early-stage BC ($P < 0.001$). The rate of receiving chemotherapy, radiotherapy, and endocrine therapy was 35.7%, 42.1%, and 50% in the illiterate group and 93.7%, 64.3%, and 71.1% in the university level education and higher group, respectively ($P < 0.001$). Moreover, the rate of breast-conserving surgery was 15.1%, 18%, 16.3%, 42.5%, and 73.2% in the illiterate, primary school level education, middle school level education, secondary school and diploma level education, and university level education and higher groups, respectively ($P < 0.001$). **Conclusion:** The study's findings showed that educational background had a significant impact on pathological staging and the selection of treatment modalities.

Keywords: *Breast cancer, educational background, pathological stage, treatment modalities*

Introduction

Among Iranian women, breast cancer (BC) is the most frequently diagnosed visceral cancer and the second cause of death based on the Cancer Registry System.[1]

There are 13,400 new BC cases annually with an incidence rate of 32 in 100000 in Iranian women. In Iran, BC was diagnosed 10 years earlier than in most developed countries. Therefore, we had significant health and treatment problems of the burden of this disease.[2]

Most breast tumors are asymptomatic, and the palpation of a lump in the breast is count as common BC symptoms. Breast tumors can appear as an abnormal pattern on a mammogram study a few months before reaching the state of being palpable by either the physician or the patient.[3]

The recent development in general awareness and educational levels, more screening mammography, and therapeutic options have resulted in enhanced early detection and the overall survival rate of women diagnosed with BC.[4]

A few studies in Western countries indicate that BC patients' educational level has a significant impact on prognosis. The reason is that patients with higher educational levels more frequently undergo screening mammography and more frequently were visited by a physician during the tumor palpation process. Therefore, the cancer is detected in earlier stage, and thus it has less pathological stage during surgery.[5-8]

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No study in Iran has investigated the association between educational levels and pathological stage, type of surgery (modified radical mastectomy [MRM] and breast-conserving surgery [BCS]), and receiving more chemotherapy, radiotherapy, and endocrine therapy in BC patients.

In this retrospective observational descriptive study, we compared educational background and its relationship with pathological stage and treatment modalities among 3010 BC patients at the Cancer Research Center of the Shahid Beheshti University of Medical Sciences between February 2001 and December 2019.

Materials and Methods

In this retrospective observational, descriptive study, a consecutive series of patients with BC (3010 patients) were identified in the database at the Cancer Research Center of the Shahid Beheshti University of Medical Sciences, a referral breast clinic in Tehran, Iran.

All the 3010 BC patients were selected based on a pathologic diagnosis with Stage I–IV. The BC staging was categorized according to the American Joint Committee on Cancer TNM System of the year 2016. All the patients were categorized based on an educational background in six levels: Illiterate, primary school level education, middle school level education, high school and diploma level education, university level education and higher, and unspecified level education.

Our exclusion criteria were BC patients who did not have a proper follow-up after initial diagnosis and patients without pathologic diagnosis. Our inclusion criteria were BC patients with Stages I–IV who had a proper follow-up after initial diagnosis and had at least seven out of 14 baseline variables (age at diagnosis, marital status, family history of BC, pathological stage of tumor, tumor histology, tumor grade, number of positive nodes, pathologic tumor size, chemotherapy, radiotherapy, endocrine therapy, estrogen receptor, progesterone receptor, and Human epidermal growth factor receptor 2 [HER2] status).

From February 2001 to December 2019, with a median follow-up time of 71 months (range 48–192 months, all the BC patients had pathologic diagnosis performed by the biopsy or surgery of the primary breast tumor. When all treatments were accomplished, each of the patients was visited and examined every 3–6 months for 5 years and yearly afterward. The patients underwent annual mammography.

In the act provided by the Shahid Beheshti University of Medical Sciences, the ethical regulations dictated were approved to review our study's medical records (ethical code: IR. SBMU.MSP.REC.1396.358). Patient consent was not required for this study because there were no anticipated risks for the study participants.

Descriptive statistics were used to summarize the baseline characteristics, clinicopathological features, and educational levels of all the patients and population's treatment modalities. Measurement data were expressed as mean ± standard deviation, and differences in all the variables were evaluated and analyzed using the Chi-square test.

Univariate logistic regression analysis was used to examine the association between education level and pathological BC stage, tumor size, and treatment modalities in the patients. In addition, multivariate logistic regression analysis was used to explore the association between age at diagnosis, educational level (middle and high school vs. primary school and below and University and above vs. primary school and below), and BC stage (Stages I and II vs. Stages III and IV). $P < 0.05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS 22.0.

Results

A consecutive series of patients with BC (3010 patients) were identified in the database at the Cancer Research Center of the Shahid Beheshti University of Medical Sciences. The average age at diagnosis was 49.1 ± 11.6 years.

Regarding education level, 4.2% (n = 126) of the patients were illiterate, 7.8% (n = 233) had primary school level education, 7.5% (n = 227) had middle school level education, 21.8% (n = 656) had secondary school and diploma level education, 18.6% (n = 560) had university level education and higher, and 40.1% (n = 1208) had unspecified level education.

Based on tumor stage, 491 cases (16.3%) were in Stage I, 1352 cases (44.9%) were in Stage II, 568 cases (18.7%) were in Stage III, 83 cases (2.7%) were in Stage IV, and 516 patients (17.1%) were in an unspecified stage.

Table 1 summarizes the patients' baseline characteristics, clinical-pathological features, and educational levels.

As of December 2019, the median follow-up time was 71 months (range 48–192 months), during which 1092 (36.3%) of the patients underwent MRM, 1580 (52.5%) of the patients underwent BCS, and 338 (11.2%) of the patients had unspecified surgery.

Of all the patients, 161 (5.4%) received neoadjuvant chemotherapy (NAC), 1625 (54%) received adjuvant chemotherapy (AC), 40 (1.3%) did not receive any chemotherapy, and 1184 (39.3%) had unspecified chemotherapy.

Of all the patients, 1927 (64%) received radiotherapy, 61 (2%) did not receive any radiotherapy, and 1022 (34%) had unspecified radiotherapy.

Of all the patients, 1596 (53%) received endocrine therapy, 1143 (38%) did not receive any endocrine therapy, and 271 (9%) had unspecified endocrine therapy.

Table 1: Baseline characteristics, clinical-pathological features and educational level of 3010 adult patients with breast cancer

Characteristics	Value (%)
Gender	
Male	0
Female	3010 (100)
Average age at diagnosis (years)	49.1±11.6
Education	
University and above	560 (18.6)
High school and diploma	656 (21.8)
Middle school	227 (7.5)
Primary school	233 (7.8)
Illiterate	126 (4.2)
Unspecified	1208 (40.1)
Family history of breast cancer	
None	1400 (46.5)
First degree	106 (3.5)
Second degree	205 (6.8)
Unspecified	1299 (43.2)
Marital status	
Married	1956 (65)
Single	124 (4.1)
Unspecified	930 (30.9)
Histological type	
Invasive ductal carcinomas	2750 (91.4)
Invasive lobular carcinomas	220 (7.3)
Others types	40 (1.3)
Tumor size (cm)	
≤2	878 (29.2)
2-5	1425 (47.3)
>5	253 (8.4)
Unspecified	454 (15.1)
Grade	
Low	256 (8.5)
Intermediate	1181 (39.2)
High	726 (24.1)
Unspecified	847 (28.2)
Lymphovascular invasion	
Positive	1204 (40)
Negative	864 (28.7)
Unspecified	942 (31.3)
Number of involved lymph nodes	
None	1133 (37.6)
1-2 involved lymph nodes	498 (16.5)
≥3	760 (25.3)
Unspecified	619 (20.6)
Stage	
Stage I	491 (16.3)
Stage II	1352 (44.9)
Stage III	568 (18.7)
Stage IV	83 (2.7)
Unspecified	516 (17.1)
ER	
Positive	1496 (49.7)
Negative	629 (20.9)
Unspecified	885 (29.4)
PR	
Positive	1413 (46.9)
Negative	712 (23.7)
Unspecified	885 (29.4)
HER2 status	
$HER2^+$	701 (23.3)
$HER2^-$	1808 (60.1)
Unspecified	501 (16.6)
Total patients	3010 (100)

ER: Estrogen receptor, HER2: Human epidermal growth factor receptor 2, PR: Progesterone receptor

Table 2 summarizes the patients' treatment modalities.

Based on the univariate logistic regression analysis, the illiterate group had 65.1% of early-stage BC (Stages I and II) and the university level education and higher group had 73.4% of early-stage BC ($P < 0.001$). Conversely, the highest (31.7%) and lowest (17.6%) rate of pathologically advanced BC (Stages III and IV) was found in the illiterate and university-level education and higher groups, respectively ($P < 0.001$). Thus, different educational backgrounds had a significant impact on final pathological staging distribution.

There were no significant differences regarding tumor size between the illiterate group with 34.2% of tumors ≤2 cm and the university level education and higher group with 29.5% of tumors ≤2 cm. Moreover, the illiterate group (6.3%) had a tumor size rate of >5 cm, which was lower than that in the university level education and higher group (8.2%) ($P = 0.145$). Thus, different educational backgrounds did not have a significant impact on final tumor size distribution.

The MRM rate was 73.8%, 70.8%, 72.7%, 46.4%, and 15.9% in the illiterate, primary-school level education, middle school level education, high school and diploma level education, and university level education and higher groups, respectively. Moreover, the BCS rate was 15.1%, 18%, 16.3%, 42.5%, and 73.2% in the illiterate, primary school level education, middle school level education, high school and diploma level education, and university level education and higher groups, respectively. Based on the univariate logistic regression analysis, these differences were statistically significant ($P < 0.001$). Thus, patients with higher education levels more frequently received BCS, whereas patients with lower education levels more frequently underwent MRM.

According to the univariate logistic regression analysis, 35.7%, 69.1%, 75.4%, 80%, and 93.7% of illiterate, primary school level education, middle school level education, high school and diploma level education, and university level education and higher groups

Table 2: Treatment modalities of 3010 adult patients with breast cancer

Characteristics	Value (%)
Surgery	
Modified radical mastectomy	1092 (36.3)
Breast conserving surgery	1580 (52.5)
Unspecified	338 (11.2)
Chemotherapy	
Neoadjuvant chemotherapy	161 (5.4)
Adjuvant chemotherapy	1625 (54)
Without chemotherapy	40 (1.3)
Unspecified	1184 (39.3)
Radiotherapy	
Done	1927 (64)
Not done	61 (2)
Unspecified	1022 (34)
Endocrine therapy	
Done	1596 (53)
Not done	1143 (38)
Unspecified	271 (9)
Total patients	3010 (100)

received chemotherapy in their treatment modalities, respectively ($P < 0.001$); the differences were significant. Thus, patients with higher education levels received more chemotherapy than patients with lower education levels in their treatment modalities.

It was shown that 42.1%, 54.5%, 60.3%, 70.7%, and 64.3% of patients in illiterate, primary school level education, middle school level education, high school and diploma level education, and university level education and higher groups received radiotherapy in their treatment modalities, respectively ($P < 0.001$). Thus, patients in the university level education and higher group received more radiotherapy than those in the illiterate and primary-school level education groups in their treatment modalities.

It was also found that 50%, 64%, 69.2%, 70%, and 71.1% of patients in the illiterate, primary school level education, middle school level education, high school and diploma level education, and university level education and higher groups received endocrine therapy in their treatment modalities, respectively ($P < 0.001$). Thus, patients with higher education levels received more endocrine therapy than those with lower education levels in their treatment modalities. These differences were significant, based on the univariate logistic regression analysis.

Table 3 summarizes univariate logistic regression analysis for the association between education level with pathological BC stage, tumor size, and treatment modalities in all the patients.

Based on the univariate logistic regression analysis, educational background had a significant impact on final pathological staging distribution. A multivariate analysis was performed with total cases of 2494 (1843 early stages [Stages I and II] vs. 651 advanced stages [Stages III and IV]) to prove whether the educational background of the BC patients was an independent factor affecting the final pathological tumor stage.

Based on the multivariable logistic regression analysis, there was no significant correlation between middle school and high school and diploma level education groups with the primary school level education group regarding the final pathological tumor stage with a 0.83 odds ratio (OR) and 95% confidence interval (CI) (0.62–1.11) ($P = 0.2$). The results suggested that education level was not an independent protective factor in the middle school, high school and diploma, and primary school level education groups.

According to the multivariable logistic regression analysis, there was a significant correlation between the university level education and higher group and the primary school level education group regarding the final pathological tumor stage with a 0.57 OR and 95% CI (0.35–0.93) ($P = 0.02$). The results suggested that education level was an independent factor affecting the final pathological tumor stage. Compared with the primary-school level education group, the university level education and higher group was an independent protective factor.

Table 4 summarizes multivariable logistic regression for the association between education level and BC stage (Stages I and II vs. Stages III and IV).

Discussion

Our findings showed that the university level education and higher group had more early-stage BC and less advanced-stage BC than the primary school level education group based on the univariate and multivariable logistic regression analysis. In the current study conducted in the Cancer Research Center of the Shahid Beheshti University, it was shown that patients in the higher education groups received more chemotherapy, radiotherapy, and endocrine therapy than patients in the lower education groups in their treatment modalities.

In the Iranian health system, most BC patients, especially those with lower educational backgrounds, demand MRM instead of BCS, indicating that more than 65% of BC patients in Iran underwent MRM. Therefore, there is a significant health and treatment problem of the burden of this disease in Iran.

Brewster *et al*. reported no significant differences regarding clinical stage between socioeconomic and educational groups. However, these findings are inconsistent with the current study, showing that patients in the higher education groups had less pathological advanced BC than patients in the lower education groups. They also found increasing tumor size in lower education groups than in higher education groups ($P = 0.02$).[9] These findings are also

Table 3: Univariate logistic regression analysis for association between education level and pathological breast cancer stage, tumor size and treatment modalities in 3010 adult patients with breast cancer

Characteristics	Illiterate (126)	Primary school (233)	Middle school (227)	High school and diploma (656)	University and above (560)	Unspecified (1208)	*P*
Surgery							
Modified radical mastectomy	93 (73.8)	165 (70.8)	165 (72.7)	304 (46.4)	89 (15.9)	447 (37)	<0.001
Breast-conserving surgery	19 (15.1)	42 (18)	37 (16.3)	279 (42.5)	410 (73.2)	628 (52)	
Unspecified	14 (11.1)	26 (11.2)	25 (11)	73 (11.1)	61 (10.9)	133 (11)	
Chemotherapy							
Done	45 (35.7)	161 (69.1)	171 (75.4)	525 (80)	525 (93.7)	498 (41.2)	0.025
Not done	2 (1.6)	3 (1.3)	3 (1.3)	6 (0.9)	5 (0.9)	18 (1.5)	
Unspecified	79 (62.7)	69 (29.6)	53 (23.3)	125 (19.1)	30 (5.4)	692 (57.3)	
Radiotherapy							
Done	53 (42.1)	127 (54.5)	137 (60.3)	464 (70.7)	360 (64.3)	578 (47.8)	<0.001
Not done	13 (10.3)	13 (5.6)	27 (11.9)	101 (15.4)	64 (11.4)	178 (14.8)	
Unspecified	60 (47.6)	93 (39.9)	63 (27.8)	91 (13.9)	136 (24.3)	452 (37.4)	
Endocrine therapy							
Done	63 (50)	149 (64)	157 (69.2)	459 (70)	398 (71.1)	595 (49.3)	<0.001
Not done	42 (33.4)	70 (30)	56 (24.7)	181 (27.6)	137 (24.5)	405 (33.5)	
Unspecified	21 (16.6)	14 (6)	14 (6.1)	16 (2.4)	25 (4.4)	208 (17.2)	
Tumor size (cm)							
≤2	43 (34.2)	79 (33.9)	67 (29.5)	193 (29.4)	165 (29.5)	329 (27.2)	0.145
2-5	55 (43.6)	106 (45.5)	99 (43.6)	299 (45.7)	224 (40)	604 (50)	
>5	8 (6.3)	19 (8.2)	19 (8.4)	66 (10)	46 (8.2)	102 (8.5)	
Unspecified	20 (15.9)	29 (12.4)	42 (18.5)	98 (14.9)	85 (15.3)	173 (14.3)	
Stage							
Stage I and II	82 (65.1)	152 (65.3)	151 (66.5)	433 (66)	411 (73.4)	725 (60)	<0.001
Stage III and IV	40 (31.7)	63 (27)	57 (25.1)	162 (24.7)	99 (17.6)	240 (19.9)	
Unspecified	4 (3.2)	18 (7.7)	19 (8.4)	61 (9.3)	50 (9)	243 (20.1)	

Table 4: Multivariable logistic regression for association between education level and breast cancer stage (Stage I and Stage II vs. Stages III and IV)

Factor	Multivariate analysis			
	Coefficient	SE	OR (95% CI)	*P*
Age at diagnosis years	−0.003	0.007	0.99 (0.98-1.01)	0.64
Middle and high school versus primary school and below	−0.19	0.15	0.83 (0.62-1.11)	0.20
University and above versus primary school and below	−0.55	0.25	0.57 (0.35-0.93)	0.02

OR: Odds ratio, CI: Confidence interval, SE: Standard error

inconsistent with the present study's findings, indicating that patients in the lower education groups did not have increasing tumor size than those in the higher educational background group ($P = 0.145$).

Macleod *et al.*'s study showed a higher rate of clinically advanced BC patients in low educational groups than in high educational groups ($P = 0.01$).[4] These findings are consistent with the present study's findings, showing that the university level education and higher group had more early-stage BC and less advanced-stage BC than the primary school level education group.

Montazeri *et al*. showed that patients in illiterate (OR 5.7, 95% CI 1.9–16.5) and primary school level education groups (OR 4.2, 95% CI 1.5–12.1) had delays in diagnosis of cancer and had more advanced stage than those in secondary school and higher-level education groups.[10] These findings are consistent with the current study's results, revealing that the highest and lowest rate of pathologically advanced BC was found in the illiterate (31.7%) and university level education and higher (17.6%) groups, respectively ($P < 0.001$).

Similarly, Grunfeld *et al.* found that patients in lower education groups had delays in diagnosis of cancer and had more advanced stage than those in higher education groups ($\chi^2 = 46.11$, df = 4, $P < 0.001$).[11] These findings are consistent with the present study, showing that the lowest and highest rate of pathologically advanced BC was found in the well-educated (17.6%) and low educated (31.7%) groups, respectively ($P < 0.001$).

In the present study, there were significant differences among the BC patients with different education backgrounds regarding their choice of surgery types. Accordingly, in the highest education group, the BSC rate was highest, while in the lowest education group, the MRM rate was highest ($P < 0.001$). These findings are consistent with Liu *et al*.' s study reporting that patients in lower education groups used more MRM and less BCS than patients in higher education groups ($P < 0.001$).[12]

Liu *et al*.' s study also showed that patients in higher education groups received more chemotherapy, radiotherapy, and endocrine therapy than those in lower education groups in their treatment modalities ($P < 0.001$). These findings are consistent with the current study's results, showing that patients in higher education groups received more chemotherapy, radiotherapy, and endocrine therapy than those in lower education groups ($P < 0.001$).

Wang *et al*. found a larger tumor size in patients in lower education groups than those in higher education groups ($P = 0.049$).[13] These findings are inconsistent with the current study's findings, as they showed that patients in lower education groups did not have a larger tumor size than those in higher education groups ($P = 0.145$). They also showed that patients in higher education groups received more chemotherapy, radiotherapy, and endocrine therapy than those in lower education groups in their treatment modalities ($P < 0.001$, $P = 0.017$, $P = 0.031$, respectively). These findings are consistent with our results showing that patients in higher education groups received more chemotherapy, radiotherapy, and endocrine therapy than those in lower education groups ($P < 0.001$).

Cantini *et al*. showed that in HER2-positive BC patients, the body mass index (BMI) influenced on pathological stage and 3-year distant disease-free survival (3-yDDFS) in negative hormone receptor (HR) BC patients. Patients with HER2+ and HR negative tumors and BMI ≥25 had shorter 3yDDFS than patients with HER2+ and HR negative tumors and BMI ≤25 (hazard ratio, 1.79; 95% CI, 1.04–3.07; $P = 0.03$).[14] One of the study's limitations was that they did not have the BMI of the BC patients.

The current study's limitations included the missing data of some of the patients (40.1% of patients would not like to give any information on their educational background) and the short follow-up period.

Conclusion

This study's findings showed that educational background had a significant impact on pathological staging and the selection of treatment modalities. These results suggest that the health ministry should focus on a group of patients with lower educational levels to develop more screening mammography, prevention, and treatment strategies for BC in this group.

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Conflicts of interest

There are no conflicts of interest.

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