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Effect of Socioeconomic Factors on Prognosis of Breast Cancer in Young Patients

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ABSTRACT
BACKGROUND: *Socioeconomic factors affect the incidence, clinical progress, and prognosis of patients with breast cancer. The aim of the study is to investigate the effect of socioeconomic factors on the prognosis of women with breast cancer at the age of forty years or younger.*
MATERIALS AND METHODS: *A total of 873 breast cancer patients were included in the study. Of these patients, 30.4% were below or at 40 years of age (n=265). Patients' clinicopathologic features and socioeconomic status (SES) were recorded. Effects of SES on clinicopathologic features were analyzed using qhi-square test. Kaplan-Meier Log Rank test was used for comparison of survival time.*
RESULTS: *Thirty percent of the patients (n=265) was at 40 years of age or younger. Median age of the patients below and over 40 years was 35 (20-40) and 52 (41-85) years, respectively. Invasive ductal carcinoma rate was found higher in younger patients with lower SES. The rate of larger tumors (>5 cm) in younger patients with lower SES was found significantly higher. Although the rate of ER and PR negative tumors was found higher (p<0.04), hormone receptor status was not found affected by SES in younger patients. Median survival time for younger patients with lower and higher SES was found 73 and 116 months, respectively (p=0.035).*
CONCLUSION: *Socioeconomic factors affect the tumor biology and clinical progress of breast cancer patients in all groups of age. Decreased overall survival among young patients with lower SES may be related to late diagnosis and/or difficulties in accessing treatment in addition to presence of unfavorable prognostic factors.*
KEYWORDS: *Breast cancer, prognostic factors, socioeconomic factors, survival, young women.*

INTRODUCTION

Breast cancer (BC) is predominantly seen in elderly people and in developed countries, only 5 to 7% of patients are diagnosed below the age of 40 years. However, in less developed regions such as Africa and the Middle East where the younger population is predominant and population-based routine screening is ineffective, BC is more common

among younger women. It is reported that approximately 20% of BC patients are younger than 40 years of age in these regions (1). In Turkey, the rate of younger patients with BC has been reported to be ~17% (2), and the rates reach up to 30% in Gaziantep and surrounding provinces (3).

The recent increase in rates of BC among young women has attracted the interest of researchers. Young age at diagnosis is reported to be an independent factor for higher relapse and poorer survival despite more aggressive therapies (1). Furthermore, higher histologic grades and unfavorable hormonal status are more common among younger BC patients (4). However, the definition of 'young' BC patient in oncology setting varies with an age scale of <35, 40, or 45 years (5). In our study, we defined 'young' patient as aged 40 years or younger.

Socioeconomic status (SES) has been established as an etiological factor for BC in addition to age, parity, family history, weight, diet, and physical activity. SES is generally defined with combinations of educational status, household income, health insurance, occupation, and ethnicity (6-8). Although BC rates are more frequent in patients with higher SES, these patients have more favorable histopathological characteristics than those with lower SES (9). In other words, lower SES is associated with worse prognosis in BC patients due to unfavorable prognostic factors(10).

Even though race/ethnicity, SES, and other sociodemographic factors are reported to affect BC survival by several studies, there are limited data explaining the association of age with these factors (11). In other respects, effect of SES on prognosis of younger BC patients is not clearly established in Turkey. In this study, we aimed to investigate the effect of SES on clinicopathological features and prognosis of BC in young patients.

MATERIALS AND METHODS

A total of 873 women with BC who attended the Department of Radiation Oncology between October 2006 and November 2015 were included in this retrospective study.

Patients' age at diagnosis, SES, clinic and pathologic features were recorded. SES is defined regarding to educational status, household income and residence (urban or rural). Patients who were illiterate, living in the rural areas and not having a regular monthly household income were grouped as lower SES. Rest of the patients were included in the higher SES group. Menopause was defined as the absence of the menses for a minimum of 12 continuous months prior to the diagnosis of BC, and the premenopausal and postmenopausal patients at the time of diagnosis were recorded. Tumor stage, tumor size, histologic grade, lymph node and hormone receptor status (estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2)) were recorded. Sociodemographic and clinical properties of the patients by age are shown in Table 1.

Statistical Analysis

Data analysis was performed using statistical analysis with the Statistical Package for the Social Sciences for Windows (SPSS, version 22.0, Chicago, IL).

Descriptive statistics were used to examine the following baseline characteristics of BC cases: age at diagnosis, histopathology, tumor grade, stage at diagnosis, hormone receptor status, household income, patients' residence, and educational status. Effects of SES on clinicopathological features were analyzed using qhi-square test. Kaplan-Meier Log Rank test was used for comparison of survival times. The results were accepted statistically significant when p-value was less than 0.05.

Table 1. Sociodemographic and clinical properties of patients by age

Variables	≤ 40 age % (n)	> 40 age % (n)	Total % (n)	*P value*
Histopathology				< .01
IDC	75.5 (200)	88.3 (537)	84.4 (737)	
NIDC	24.4 (65)	11.7 (71)	15.6 (136)	
Histologic grade				< .02
I	2.6 (7)	6.3 (38)	5.2 (45)	
II	38.1 (101)	43.1 (262)	41.6 (363)	
III	52.1 (138)	42.1 (256)	45.1 (394)	
Unknown	7.1 (19)	8.6 (52)	8.1 (71)	
Disease stage				0.1
I	4.2 (11)	5.1 (31)	4.8 (42)	
II	37.4 (99)	44.7 (272)	42.5 (371)	
III	47.2 (125)	40.3 (245)	42.4 (370)	
IV	11.2 (30)	9.9 (60)	10.3 (90)	
ER status				< .001
ER+	57 (151)	72.2 (439)	67.6 (590)	
ER−	37.4 (99)	26.6 (162)	29.9 (261)	
Unknown	5.6 (15)	1.2 (7)	2.5 (22)	
PR status				< .001
PR+	63 (167)	70.7 (430)	68.4 (597)	
PR−	31 (82)	27.8 (169)	28.8 (251)	
Unknown	6 (16)	1.5 (9)	2.8 (25)	
HER2 status				0.8
HER2+	36.2 (96)	31.6 (192)	33 (288)	
HER2−	60.4 (160)	66.8 (406)	64.8 (566)	
Unknown	3.4 (9)	1.6 (10)	2.2 (19)	
Education level				< .001
None	26.7 (71)	53.8 (327)	45.6 (398)	
Primary school	45.7 (121)	29.3 (178)	34.2 (299)	
Junior-high school	7.2 (19)	5.6 (34)	6.1 (53)	
High school	9.1 (24)	7.2 (44)	7.8 (68)	
University	11.3 (30)	4.1 (25)	6.3 (55)	
Residence				0.02
Urban	86 (228)	79.4 (483)	81.4 (711)	
Rural	14 (37)	20.6 (125)	18.6 (162)	
Household income <600 USD				< .03
600–1600 USD	26.8 (71)	21.4 (130)	23 (201)	
>1600 USD	41.1 (109)	37.3 (227)	38.5 (336)	
	32.1 (85)	41.3 (251)	38.5 (336)	

IDC, invasive ductal carcinoma; NIDC, non-invasive ductal carcinoma; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor-2; USD, United States Dollar

RESULTS

The majority of patients with BC were premenopausal (59.2%, n=517). Thirty percent of the patients (n=265) was at 40 years of age or younger. Median age of the patients below and over 40 years was 35 (20-40) and 52 (41-85) years, respectively.

There was an association between tumor histopathology and SES. Invasive ductal carcinoma (IDC) rate was found higher in younger patients with lower SES (Table 2). While the IDC rate in illiterate younger patients was 84.4% (n=54), it was 65.5% in patients who graduated from university (n=19, p<0.04). Furthermore, IDC rates for rural and

urban residents were 89.2% (n=33) and 73.2% (n=167), respectively (p=0.037).

Tumor size was also associated with SES. The rate of larger tumors (>5 cm) in younger patients with lower SES was found significantly higher. The rates of larger tumors in patients with lower and higher SES were 53.5% (n=38) and 37.2% (n=72), respectively (p<0.001).

Additionally, advanced stage was found associated with lower SES in younger patients (p<0.001) (Table 2).

Table 2. Clinical properties of patients by age and socioeconomic status

Variables	Low SES % (n)		High SES % (n)		P value
	≤ 40 age	> 40 age	≤ 40 age	> 40 age	
Histopathology					< 0.04
IDC	87.7 (57)	89.2 (116)	71.5 (143)	88.3 (421)	
NIDC	12.3 (8)	10.8 (14)	28.5 (57)	11.7 (56)	
Tumor size					< .001
< 2 cm	4.2 (3)	6.9 (9)	10.8 (21)	11.3 (54)	
2-5 cm	35.2 (25)	43.8 (57)	51 (99)	59.8 (286)	
> 5 cm	53.5 (38)	46.9 (61)	37.2 (72)	27.2 (130)	
Unknown	7.1 (5)	2.3 (3)	1 (2)	1.7 (8)	
Lymph node status					<. 001
Positive	82.5 (61)	74.1 (100)	68.6 (131)	69.2 (327)	
Negative	6.7 (5)	18.5 (25)	28.3 (54)	28.1 (133)	
Unknown	10.8 (8)	7.4 (10)	3.1 (6)	2.7 (13)	
Disease stage					< .001
I	0 (0)	3.1 (4)	5.7 (11)	5.6 (27)	
II	21.1 (15)	33.1 (43)	43.3 (84)	47.9 (229)	
III	63.4 (45)	53.1 (69)	41.2 (80)	36.8 (176)	
IV	15.5 (11)	10.8 (14)	9.8 (19)	9.6 (46)	
Grade					> 0.6
	2.8 (2)	6.9 (9)	2.6 (5)	6.1 (29)	
II	33.8 (24)	41.5 (54)	39.7 (77)	43.5 (208)	
III	56.3 (40)	45.4 (59)	50.5 (98)	41.2 (197)	
Unknown	7 (5)	6.2 (8)	7.2 (14)	9.2 (44)	
ER status					> 0.07*
ER+	53.5 (38)	65.4 (85)	58.2 (113)	74.1 (354)	
ER-	38 (27)	33.6 (44)	37.2 (72)	24.7 (118)	
Unknown	8.5 (6)	1 (1)	4.6 (9)	1.2 (6)	
PR status					0.06*
PR+	67.6 (48)	58.3 (76)	61.3 (119)	74.1 (354)	
PR-	23.9 (17)	40.7 (53)	33.5 (65)	24.3 (116)	
Unknown	8.5 (6)	1 (1)	5.2 (10)	1.6 (8)	
HER2 status					> 0.6
HER2+	45.1 (32)	33.8 (44)	33 (64)	31 (148)	
HER2-	50.7 (36)	64.6 (84)	63.9 (124)	67.4 (322)	
Unknown	4.2 (3)	1.5 (2)	3.1 (6)	1.7 (8)	

IDC, invasive ductal carcinoma; NIDC, non-invasive ductal carcinoma; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor-2
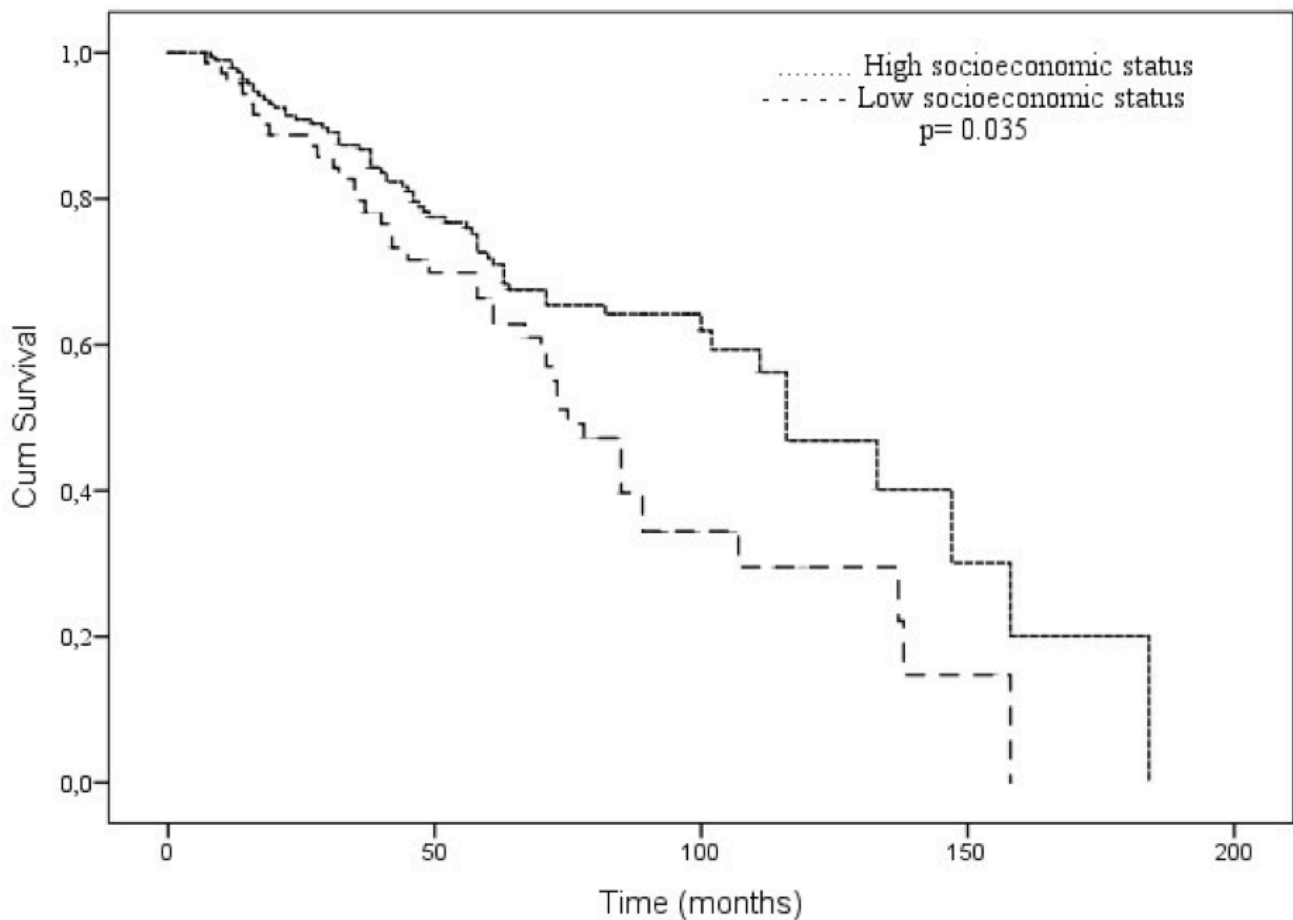
Figure 1. Survival curve by socioeconomic status in young patients with breast cancer

Rate of grade 3 tumors was higher in younger patients (n=138) compared to elderly ones (n=256), (52.1% vs. 42.1%, p<0.02). However, SES had no impact on tumor grade in younger patients (p>0.6, Table 2).

Although rate of ER and PR negative tumors was found higher in younger patients (p<0.04), hormone receptor status was not found affected by SES in younger patients (Table 2).

Overall survival was shorter in patients with lower SES. The median survival time was 107 months for younger patients, and 137 months for patients over 40 years of age (p=0.013). Among younger patients, median survival time was 111 months in urban residents and 100 months in rural residents (p=0.01). Median survival time for younger patients with lower and higher SES was found 73 and 116 months, respectively (p=0.035) (Figure 1).

DISCUSSION

Breast cancer is predominantly a disease of elderly women and the rate of BC patients diagnosed below the age of 40 years in developed countries are only 5 to 7%, however, in contrast to developed countries, incidence of BC is more frequent among young women in less developed regions of the world (1). Young BC patients are known to have worse prognosis due to advanced

tumor stage at diagnosis, hormone receptor negativity, higher histological grade, abnormal p53 expression, overexpression of HER2, and increased rates of involved lymph nodes and lymphovascular invasion (12, 13).

It is well established that SES is one of the instances which is associated with increased risk of BC. Patients with lower SES are commonly premenopausal and tend to have aggressive disease with more advanced stage at diagnosis and poorer survival (14). Reports from a large number of studies stated that BC survival was associated with race/ethnicity, SES, and certain sociodemographic factors, however, there is limited data about the effect of these factors on patients diagnosed at younger age(11). Association between SES and BC prognosis among young women is still unclear in our country, therefore, we aimed to investigate the effect of SES on younger BC patients. Educational status, living area and household income were included in the study to determine SES and we found that SES influenced clinicopathological features and prognosis of the younger BC patients. Unfavorable prognostic factors such as larger tumor size, increased lymph node metastasis and advanced stage were more common in younger patients with lower SES. Additionally, these patients had shorter survival.

In previous studies, although larger tumor size was associated with lower SES in BC patients, a significance of histopathology was not reported in younger patients (9). However, in the study of Thomson et al., SES was not found to affect neither tumor size nor tumor histopathology (15). Unlike these studies, we found that SES had an effect on tumor histopathology in our study. While the rates of IDC were higher among younger illiterate and rural resident patients, non- IDC rates were higher in educated patients living in urban areas. Tumor size was also found significantly affected by SES in the study; T3 and T4

tumors were more common in younger patients with lower SES.

Lower SES is associated with advanced stage and shorter survival time (6, 7, 16). Consistent with previous studies, in our study, younger patients with lower SES were diagnosed at more advanced stage with higher metastases to lymph nodes. These findings may be explained by the unawareness of disease in patients with lower educational status and delayed medical support to the rural residents.

Lower SES has been associated with higher tumor grade, overexpression of HER2 and higher rates of hormone receptor negativity in previous studies (8, 9, 17, 18). Hormone receptor status is an important prognostic factor affecting the survival of BC patients. Hormone receptor-negative BC is strongly associated with worse prognosis. Howlader et al. reported that patients with lower SES had higher rates of hormone receptor-negative BC (19). Thomson et al. reported that women with lower income had higher rates of ER-negative tumors and worse treatment results (15). Although grade 3 tumors and ER/PR negative subtypes were more common among younger patients in the present study, these were not significantly associated with SES.

While shorter survival for the patients with lower SES is mostly related to the advanced disease at diagnosis and poorer health status, only in a little group of patients it is associated with variations in cancer care (20). However, BC patients living in urban areas are likely to have higher SES and decreased cancer-related death risk (16, 21, 22). In the study, we found that the patients with higher SES or living in urban areas had longer survival irrespective of age. Prognostic factors such as tumor size and stage were adversely influenced by lower SES and resulted in decreased survival in younger BC patients.

CONCLUSION

Premenopausal and younger BC patient rates were high in Gaziantep and surrounding provinces compared to the worldwide incidence. Decreased overall survival among young patients with lower SES may be related to late diagnosis and/or difficulties in accessing treatment in addition to the presence of unfavorable prognostic factors. Further studies with larger number of patients are needed to support these findings.

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