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Association Between Triple-Negative Breast Cancer and Socioeconomic and Cultural Factors in Southeast Anatolia: A Single-Center Experience

Güneydoğu Anadolu'da Triple Negatif Meme Kanseri ile Sosyoekonomik ve Kültürel Faktörler Arasındaki İlişki: Tek Merkez Deneyimi

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Abstract

Objective: Triple-negative breast cancer (TNBC) is associated with younger age, advanced stage at diagnosis, ethnicity, lower socioeconomic status (SES), and poor prognosis. The aim of the study was to investigate clinicopathologic features of TNBC patients living in Southeast Anatolia, and the association between socioeconomic and cultural factors and TNBC.

Material and Method: A total of 875 women were included in the study. Patients' age at diagnosis, living area (rural or urban), SES, ethnicity (Arabic, Armenian, Kurdish, and Turkish) and clinicopathologic features were recorded. SES of the patients was categorized as lower and higher according to educational and health insurance status, and household income. Patients who were illiterate and did not have a health insurance and regular monthly household income were grouped as lower SES. Effects of SES on clinicopathologic features of the patients with TNBC were analyzed using qhi-square test. The difference in survival across strata was compared with the Log-Rank test.

Results: Ten percent of the patients (n=87) were diagnosed with TNBC. Median age at diagnosis for patients with TNBC and non-TNBC was 44 years (24-84) and 47 years (20-85), respectively. TNBC rates were higher in patients ≤ 40 years. Younger age, lower SES, and Arabic and Kurdish ethnicities were associated with higher rates of TNBC ($P < 0.04$).

Conclusion: Although the majority of the breast cancer patients living in Southeast Anatolia were premenopausal, the rate of TNBC among them was found lower than the general rate of western countries. Socioeconomic and cultural factors may affect tumor biology and prognosis of the disease in patients with TNBC. In our study, younger age, lower SES, and ethnicity were associated with higher rates of TNBC and worse prognosis.

Keywords: Triple-negative breast cancer, socioeconomic factors, prognosis

Öz

Amaç: Triple negatif meme kanseri (TNMK) genç yaş, tanı anında ileri evre hastalık, etnik köken, düşük sosyoekonomik statü (SES) ve kötü prognozla ilişkilidir. Bu çalışmanın amacı Güneydoğu Anadolu'da yaşayan triple negatif meme kanserli hastaların klinikopatolojik özelliklerinin yanı sıra TNMK ile sosyoekonomik ve kültürel faktörler arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Toplam 875 hasta çalışmaya dâhil edildi. Hastaların tanı anındaki yaşı, klinikopatolojik özellikleri, yaşadıkları bölge (kırsal veya kentsel), SES ve etnik kökenleri (Arap, Ermeni, Kürt, Türk) kaydedildi. Hastaların SES'i, eğitim düzeyi, aylık gelirleri ve sağlık güvencesi durumuna göre düşük ve yüksek olmak üzere ikiye ayrıldı. Düşük SES grubuna okur-yazar olmayan, sağlık sigortası ve düzenli aylık geliri olmayan hastalar alındı. TNMK'li hastaların klinikopatolojik özellikleri üzerine SES'in etkisini analiz için Ki-kare testi kullanıldı. Log-Rank testi kullanılarak sağ kalım analizi yapıldı.

Bulgular: Hastaların %10'unda (n=87) TNMK tanısı mevcuttu. Medyan tanı yaşı TNMK olan hastalarında 44 (24-84) ve TNMK olmayan hastalarında ise 47 (20-85) olarak bulundu. TNMK oranları 40 yaş ve altındaki hastalarda daha fazlaydı. Genç yaş, düşük SES ve Arap ile Kürt etnik kökenlilerde TNMK oranları daha yüksek bulundu ($P < 0,04$).

Sonuç: Güneydoğu Anadolu bölgesindeki hastaların çoğunluğu premenopozal olmasına rağmen TNMK oranları batılı ülkelerdeki oranlardan daha düşük bulunmuştur. Sosyoekonomik ve kültürel faktörler TNMK olan hastalarda tümör biyolojisini etkileyebilmektedir. Genç yaş, düşük SES ve etnik kökenin daha yüksek TNMK oranları ve daha kötü prognozla ilişkili olduğu bulunmuştur.

Anahtar Kelimeler: Triple negatif meme kanseri, sosyoekonomik faktörler, prognoz

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INTRODUCTION

Triple-negative breast cancer (TNBC) is a term defining tumors lacking estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2), and is a rare subtype of breast cancer (BC). TNBC is commonly seen among young women and known to have a worse prognosis, and develops early metastasis despite optimal treatment.[1] Although clinical data about TNBC is limited in Turkey, studies performed in developed countries have established that TNBC is more common in patients with younger age and advanced stage at diagnosis, and is also related to race/ethnicity, lower socioeconomic status (SES), and poorer survival outcomes.[2]

In addition to environmental factors and lifestyle, socioeconomic cultural factors (SECFs) may also affect the frequency of TNBC and the prognosis of the disease.[3] While the effects of these factors on TNBC are well established in western countries, to our knowledge, there is no study investigating this subject in Turkey.

In our study, clinicopathologic features of women with TNBC living in Southeast Anatolia and the association between TNBC and SECFs were investigated.

MATERIAL AND METHOD

A total of 875 women with BC who attended the Department of Radiation Oncology between November 2006 and July 2015 living in Gaziantep and nearby cities were evaluated for the study. The study was approved by the local ethics committee (Date: 04.09.2008, Decision Number: 2008/2560) and conducted by principles of the Helsinki Declaration 2008. Patients were informed and approved consent forms were obtained.

Patients' age at diagnosis, living area (rural or urban), ethnicity (Arabic, Armenian, Kurdish and Turkish), educational and health insurance status, and household income were recorded.

Patients were divided into two groups as lower and higher SES according to educational and health insurance status, and household income. Patients who were illiterate and did not have a health insurance and regular monthly household income were grouped as lower SES. Patients' data were obtained by asking them verbally and recorded by medical staff. Demographic and clinicopathologic features of the patients were obtained from medical reports. Two Armenian patients with hormone receptor negative BC (one of them was HER-2 positive) were excluded from the statistical analysis, as the number in this subgroup was inadequate to evaluate.

Statistical analyses

Examination of the BC characteristics such as age at diagnosis, ethnicity, stage, and status of triple negativity were constructed by using descriptive statistics. The $\chi 2$ test was used to compare the frequency of distributions between subgroups for categorical variables. The difference in survival across strata was compared with the Log-Rank test. Univariate and multivariate Cox regression analysis was used to determine the factors associated with survival. All P values were two-sided, and P value < 0.05 was accepted statistically significant. Statistical Package for Social Sciences (SPSS) for Windows 23.0 IBM SPSS Statistics, New York, USA was used for statistical analyses.

RESULTS

The majority of the patients were premenopausal in all of the study population, and premenopausal and postmenopausal patient rates were 59.2% (n=518) and 40.8% (n=357), respectively. Ten percent (n=87) of the patients were diagnosed with TNBC. The median age at diagnosis for patients with TNBC and non-TNBC was 44 (24-84) and 47 (20-85) years, respectively.

Age at diagnosis, ethnicity and SES were found to affect rates of TNBC. TNBC rates were higher in patients ≤ 40 years of age than in patients > 40 years [13.7% (n=36) vs. 8.5% (n=51), (P < 0.02)]. Lower SES, and Arabic and Kurdish ethnicities were associated with higher rates of TNBC (P < 0.04). Patients' demographic and clinicopathologic features are shown in **Table 1**.

Table 1. Patients' characteristics according to the tumor subtypes

Characteristics	Total* % (n)	Tumor subtypes		P value†
		Triple negative % (n)	Non-Triple negative % (n)	
Histological type				0.09
Invasive ductal	84.5 (732)	77.3 (68)	85.4 (665)	
Non-invasive ductal	4.8 (41)	5.7 (5)	4.6 (36)	
Unknown	10.7 (93)	17 (15)	10 (78)	
Tumor size				0.5
> 2 cm	87.9 (761)	89.6 (78)	87.7 (683)	
≤ 2 cm	10 (87)	6.9 (6)	10.4 (81)	
Unknown	2.1 (18)	3.5 (3)	1.9 (15)	
Histological grade				0.015
Grade I-II	46.8 (405)	32.2 (28)	48.4 (377)	
Grade III	45.1 (391)	58.6 (51)	43.6 (340)	
Unknown	8.1 (70)	9.2 (8)	8 (62)	
Stage				0.3
Early (I-II)	47.3 (410)	52.8 (46)	46.7 (364)	
Locally advanced (III)	42.4 (367)	34.5 (30)	43.3 (337)	
Metastatic (IV)	10.3 (89)	12.7 (11)	10 (78)	
Education				0.05
None	45.5 (394)	55.2 (48)	44.4 (346)	
Primary-JHS	40.2 (351)	32.2 (28)	41.5 (323)	
HS-University	14.3 (121)	12.6 (11)	14.1 (110)	
Socioeconomic status				0.037
Low	23.2 (201)	32.2 (28)	22.2 (173)	
High	76.8 (665)	67.8 (59)	77.8 (606)	
Residence				0.4
Urban	18.6 (161)	21.8 (19)	18.2 (142)	
Rural	81.4 (705)	78.2 (68)	81.8 (637)	
Ethnicity				0.03
Turkish	69.6 (603)	57.5 (50)	71 (553)	
Kurdish	24.6 (213)	33.3 (29)	23.6 (184)	
Arabic	5.8 (50)	9.2 (8)	5.4 (42)	

*Triple negative status of 7 patients is unknown, †Chi-square test was performed, HS; high school, JHS; junior high school

In patients with TNBC, Arabic and Kurdish ethnicity, and lower SES were found to be associated with larger tumor sizes (P < 0.02). Tumor characteristics of patients with TNBC are summarized in **Table 2**. Furthermore, SECFs such as younger age, lower SES, and Arabic and Kurdish ethnicity were found to worsen survival of the patients with TNBC (P < 0.03, **Table 3**).

Table 2. Tumor characteristics of TNBC patients

Variables	Ethnicity % (n)			SES % (n)		P value
	Turkish	Kurdish	Arabic	Low	High	
Tumor size						<0.02
≤2 cm	74 (37)	55.1 (16)	50 (4)	39.2 (11)	78 (46)	
>2 cm	26 (13)	44.9 (13)	50 (4)	60.8 (17)	22 (13)	
LNS						<0.05*
Positive	64 (32)	62 (18)	62.5 (5)	77.8 (22)	57.9 (33)	
Negative	36 (18)	38 (11)	37.5 (3)	22.2 (6)	42.1 (24)	
Stage						
I-II	62 (31)	41.4 (12)	37.5 (3)	25 (7)	66.1 (39)	<0.04
III	26 (13)	48.3 (14)	37.5 (3)	60.7 (17)	22 (13)	
IV	12 (6)	10.3 (3)	25 (2)	14.3 (4)	11.9 (7)	
Tumor grade						>0.4
Grade I-II	34 (17)	27.6 (8)	37.5 (3)	21.4 (6)	37.3 (22)	
Grade III	66 (33)	72.4 (21)	62.5 (5)	78.6 (22)	62.7 (37)	

* No significant difference was found between ethnic groups. LNS; Lymph node status, TNBC; triple negative breast cancer, SES; socioeconomic status

Table 3. Mean survival time for patients with TNBC

	Mean				
	Time (months)	Std. Error	95% Confidence Interval		P value*
			Lower Bound	Upper Bound	
Age					0.02
≤ 40	77	10,737	55,955	98,042	
> 40	104	8,003	88,065	119,435	
Ethnicity					0.017
Turkish	104	8,594	87,056	120,744	
Kurdish	61	8,475	44,390	77,613	
Arabic	78	9,551	58,780	96,220	
SES					0.028
Low	64	8,649	46,876	80,782	
High	103	8,053	86,725	118,295	

*Long rank test was performed. SES; socioeconomic status, TNBC; triple negative breast cancer

Patients with TNBC were found to have poorer overall survival (OS). Median OS for patients with TNBC and non-TNBC was 90 months (95% CI: 79-105 months) and 130 months (95% CI: 108- 150 months), respectively (P=0.015). Besides triple negativity, OS was also affected by stage, ethnicity, age and SES (**Table 4**).

Table 4. Cox regression analysis for overall survival

Variables	Univariate P value	Multivariate P value	Hazard rate	95% Confidence interval	
				Lower	Upper
TN vs NTN	0.016	0.027	0.679	0.482	0.957
Age (≤40 vs >40)	0.008	0.015	1.353	1.062	1.724
Stage	< 0.001	0.001	2.608	2.199	3.092
Ethnicity	0.001	0.007	1.856	1.026	4.423
SES	< 0.001	0.003	1.683	1.075	2.290

SES; socioeconomic status, TN; triple negative, NTN; non-triple negative

DISCUSSION

Risk factors of BC may be categorized as biological and non-biological (e.g. lifestyle of the patient). Both of these factors are related to the prognosis of patients with BC.[4] While tumor biology of BC has a complex process, SECFs which are among the non-biological factors may also influence clinic features of the disease either positively or negatively.[5] The interaction of SECFs with TNBC incidence and prognosis are well established in western countries. However, to our knowledge, the effect of these factors on TNBC is not thoroughly investigated in Turkey. In our regional single-center study, we focused on the effect of these factors on TNBC and found that SECFs affect rates of TNBC. Moreover, the prognosis was also affected by SES and ethnicity according to our findings.

The incidence of TNBC is higher among younger patients.[6] Patients diagnosed with TNBC at younger ages have a poorer prognosis compared to older ones.[7] Incidence of TNBC may vary according to geographical locations and SECFs. In Turkey, TNBC rates are reported to be approximately 10 to 28% of BCs. However, the incidence of TNBC may vary between regions of Turkey.[8-10] Despite the increased rates of premenopausal BC in Southeast Anatolia, there was an unexpected decrease in the rates of TNBC. In the current study, the rate of TNBC was found as 10% of the patients. TNBC rates were found to be increased in younger patients compared to older ones (P < 0.02, **Table 1**). According to our study results, the prognosis of the TNBC was also worse in younger patients as expected (**Table 3**).

It is well established that SECFs influence the risk of development of TNBCs.[11] Lower SES is reported to be associated with advanced stage at diagnosis, worse prognosis, and poorer survival in women with premenopausal BC and TNBC.[3,11] The disparities in the survival of patients with TNBC regarding SES, ethnicity, educational status, and access to health insurance and preventive care are well established.[11] Although we reported in our previous study that SECFs might affect clinicopathologic features of BC, the effects of SECFs on TNBC are not clearly defined in Turkey. In the present study, younger age, lower SES, Arabic and Kurdish ethnicity, and advanced disease at diagnosis were found to affect

prognosis negatively (**Table 4**). Additionally, lower SES was found to be associated with TNBC incidence. While patients' residence location, marital status, number of pregnancies, and births did not affect the rates of TNBC, their educational status did. The rate of TNBC was found significantly higher in illiterate patients (**Table 1**).

Several studies reported that there are racial disparities among the patients diagnosed with TNBC (e.g. 2- or 3-fold increased risk in Black Americans).[12] Beside African American race/ethnicity, association between TNBC and younger age, poorly differentiated tumor, advanced stage at diagnosis, and poorer survival were also reported.[3] (3) In the present study, TNBC rates were not significantly different between Kurdish and Arabic patients, however, were significantly higher in both ethnicities compared to Turkish patients ($P < 0.04$). Additionally, Arabic and Kurdish women with TNBC were diagnosed at more advanced stage compared to Turkish women, and had larger primary tumors than Turkish women (**Table 2**).

Outcomes may vary with different phenotypes of BC and the TNBC has the worst prognosis compared to other histopathological subtypes. Patients with TNBC were shown to have poorer disease-free survival and overall survival than the rest of BC patients in previous studies.[9] Similarly, patients with TNBC had shorter survival compared to other BC subtypes in our study. Furthermore, younger age, lower SES, and Arabic and Kurdish ethnicities were found to be associated with poorer survival in patients with TNBC.

CONCLUSION

Although the majority of the BC patients in Southeast Anatolia were premenopausal, the rate of TNBC among them was found lower than the average rate of western countries. It was determined that SECFs influenced clinical and biological findings of TNBC. Lower SES was associated with a worse prognosis in patients with TNBC. Additionally, Arabic and Kurdish women with TNBC in the study had worse survival than Turkish ones, although they were managed with similar modalities.

The factors affecting survival regarding SECFs and ethnicity remain unclear in the rest of the Turkey. Further epidemiological and genetic studies are required to support the findings of the current study.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ethical Committee of Gaziantep University, School of Medicine (Date: 04.09.2008, Decision No: 2008/2560).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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