GEOGRAPHICAL DISTRIBUTION AND TRENDS OF WOMEN BREAST CANCER MORTALITY IN TURKEY BETWEEN 2009-2019

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Abstract

Objectives: Breast cancer is the most common malignancy in women all over the World. It is in the first line, causing deaths because of cancer in women worldwide. However, its progress differs regarding the counties' socioeconomic and cultural features. The aim of this study is to estimate breast cancer mortality rates in Turkish women by geographic region and to evaluate 11-year mortality trends.

Materials and Methods: Joinpoint Regression Analysis was used to estimate the trends of mortality from breast cancer by gender and age groups for every geographic region. Also, we used the world standard population (100,000 women) was used to estimate the age-standardized mortality rates as a reference to calculate age-standardized mortality rates.

Results: We found that nearly 39,000 women died from breast cancer between the years 2009-2019. During this 11-year period, the age-standardized mortality rate in Turkey was 6.84 per 100,000 women in 2009, while it rose up to 8.16 in 2019 with a significant increase of 1.78 per year (Confidence Interval: 0.57:3.00) p=0.009). This change was observed especially in TR2, TR7, TR9, TRA, TRB and TRC regions. According to the age groups examined, significant increases were observed in all age groups in Turkey.

Conclusion: Breast cancer is still a very important health problem in Turkish women of all ages. It is essential to take measures to reduce the breast cancer mortality rate and increase early diagnosis opportunities in our country.

Keywords: Breast cancer, mortality rate, joinpoint regression analysis.

Introduction

In the World, cancer is the most common cause of death worldwide. It caused approximately 10 million deaths in 2020. Cancer was found to be the most common cause of mortality in 57 of 127 nations analyzed, including Turkey. According to the same research, by the turn of the century, cancer-related deaths will rise and overtake all other causes of early death in the majority of countries.[3]

Breast cancer is the most commonly diagnosed cancer in terms of new cancer cases in 2020. It is the most important public health problem, leading to the most frequent cancer-related deaths among women worldwide. In 2020, the World Health Organization reported that there were 2.2 million (25.4%) cases of breast cancer in women, and in the same year, globally, breast cancer-related deaths accounted for 15.5% (684 996) of total deaths.[1] The World Health Organization predicts that the incidence and deaths of breast cancer in women will double by 2040.[2]

Due to delayed diagnosis and limited access to cancer care, breast cancer survival rates in low- and middle-income countries are lower than those in high-income nations. Because of improvements in prevention, screening, and treatment, there have been fewer fatalities from cancer in several parts of the world, particularly in high-income nations. In 12 different parts of the world, breast cancer also ranks first in terms of cancer deaths.[1]

Breast cancer was identified as the leading cause of death for women in a 2020 study carried out in Turkey. The study indicates that the incidence of breast cancer has increased over time.[4] When only taking into account deaths in city and district centers between 1987 and 2008, the average annual standardized death rate was reported by Doğan et al. in 2014 to be 11.9 (per 100,000 women).[5] According to Teker et al.'s study, there has been an increase in cancer-related fatalities in recent years.[5,6] According to Li, one of the most significant indicators for tracking the health of breast cancer patients is mortality.[7] Trend analysis is a method for determining patterns of change or trends in a variety of observations, both globally and locally, in order to guide local control methods.

This study aimed to evaluate trends in breast cancer death rates among women in Turkey over time by years, age groups, and geographic regions.

Materials and Methods

An ecological study was carried out, taking into account all women breast cancer fatalities that occurred in Turkey from 2009 to 2019. The Turkish Statistical Institute has been compiling and publishing annual death

records at the national level in Turkey since 1931. Prior to 2009, only the province and district centers were included in the death records; however, in the years that followed, the death lists from the villages were added, and the entire country of Turkey was covered. The International Classification of Diseases, Tenth Revision (ICD-10) has also been utilized since 2009 in the classification system for causes of death.[8] The C50 code from the ICD-10 revision was used to assess the cause of death from breast cancer in women. Statistical information on breast cancer deaths is available from 2009 to 2019 and is segmented by year and age in 12 areas for each year in 5 age groups up to 85+ years.

Data from TurkStat is based on the death notification system and previous data generated by the Ministry of Health, General Directorate of Public Health. The breast cancer mortality data was obtained through an official request to the relevant institution, which did not impose any restrictions on information sharing and analysis. For this reason, ethics committee approval was not received.

The General Directorate of Public Health of the Ministry of Health and prior data are the foundations for TurkStat's statistics. Data on breast cancer deaths were obtained by asking for an official petition from the relevant institution; no restrictions were placed on the sharing and analysis of information.[9] Specific rates were calculated for different age groups (<45, 45-54, 55-64, 65-74, and 75+) based on data on deaths considering year and region.

Age-standardized mortality rates (ASMR) were calculated using the direct standardization approach and the world standard population as a reference. Rates are given in terms of fatalities per 100,000 people. For the age range of 0 to 85, age-specific mortality rates were computed across 5-year intervals. By accounting for population age structure variations, this method eliminates the impact of historical events on the age structure and is used to compare different cities or nations.[10] For each region, the same strategy was employed.

Statistical analysis

A statistical modeling method called Joinpoint Regression Analysis (JRA) uses piecewise linear regression to describe the relationship between two variables. In epidemiological studies, this method is frequently used to model time trends in mortality or incidence series. In the JRA, the change point is defined as a "joinpoint," and in 2000, the Grid Serch method proposed by Lerman was used to find these change points by Kim et al.[11] The analysis starts with the minimum point of change and tests each time whether the change point is significant and should be added to the model. The number of change points is determined by the Monte Carlo Permutation test.[11] The final model obtained shows optimal changeover points where the ratio does/is not significantly changed. For each statistically significant change point, annual percentage change (APC), average annual percentage change (AAPC), and their 95% confidence intervals (CI) are calculated. AAPC is the average of the APC values at all breakpoints. Analyzes were performed using the Joinpoint Regression Program (version

4.9.1.0–2021) prepared by the US National Cancer Institute (National Cancer Institute, 2021). A value of P<0.05 was considered statistically significant.

Nomenclature of Territorial Units for Statistics (NUTS): In order to gather and develop regional data, analyze the socioeconomic makeup of the regions, set regional policies, and create a database that can be compared to the European Union Regional Statistical System, NUTS definitions are created (Figure 1).
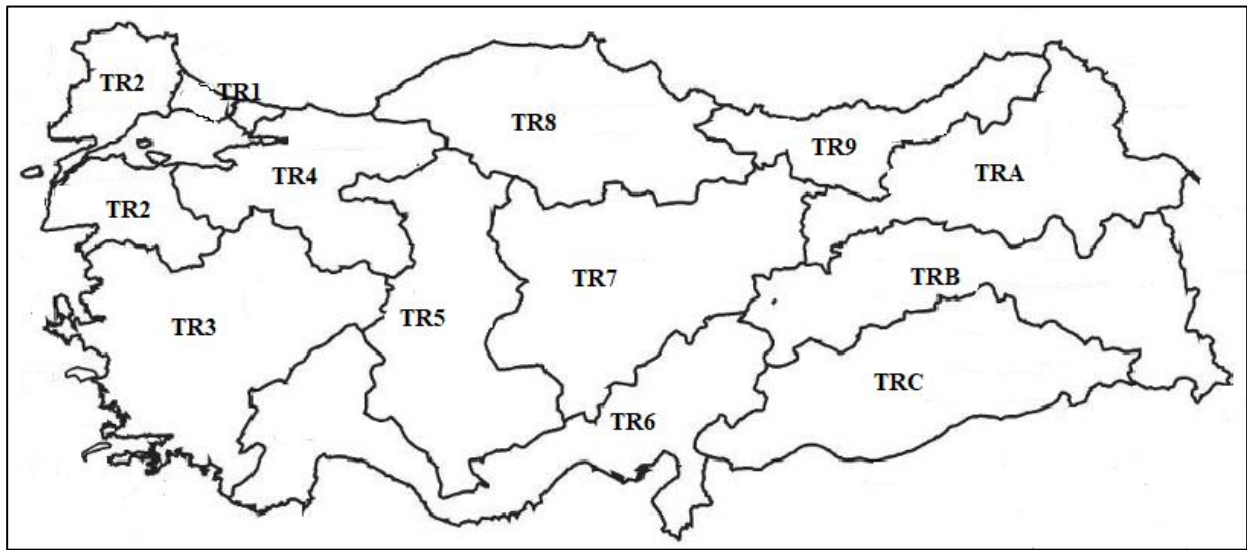
Figure 1. 12 regions in NUTS1 in Turkey

Region Classification of Nomenclature of Territorial Units for Statistics definitions is created in order to gather and develop regional data, analyze the socioeconomic make of the regions, create regional policies, and create a database that can be compared to the Regional Statistical System of the European Union. Figure 1 depicts of Turkey's 12 regions (TR1-Istanbul; TR2- Western Marmara; TR3- Aegean; TR4- Eastern Marmara; TR5- Western Anatolia; TR6- Mediterrenian; TR7- Central Anatolia; TR8- Western Black Sea; TR9- Eastern Black Sea; TRA- Northeastern Anatolia; TRB- Central Eastern Anatolia; TRC- Southeastern Anatolia.

Results

In Turkey, approximately 39000 women died from breast cancer in the period of 2009-2019. The ASMR rose from 6.84/100,000 in 2009 to 8.16/100,000 in 2019. When evaluated according to regions, annual ASMR increases were 2.28 in the TR1 region, 4.03 in the TR7 region, 2.94 in the TR9 region, 4.71 in the TRA region, 5.63 in the TRB region and 4.26 in the TRC region (Table 1).

Table 1. Age-standardized mortality rate and average annual percentage change (AAPC) of women breast cancer mortality according to region and year, 2009:2019.

Region	ASMR			
	2009	**2019**	**AAPC**	**95%CI**
TR1	10.60	10.14	-0.44	-1.65;0.80
TR2	6.63	8.75	2.81*	0.48;5.20
TR3	6.65	7.76	1.56	-0.55;3.70
TR4	8.08	9.19	1.30	-0.84;3.50
TR5	7.79	8.24	0.56	-0.44;1.58
TR6	6.52	7.87	1.89	-0.25;4.08
TR7	5.04	7.47	4.03*	0.62;7.55
TR8	5.66	6.23	0.96	-1.05;3.10
TR9	4.92	6.59	2.94*	0.23;5.73
TRA	4.51	7.22	4.71*	0.98;8.57
TRB	4.19	7.42	5.63*	2.48;8.88
TRC	3.77	5.71	4.26*	0.02;8.67
Turkey	6.84	8.16	1.78*	0.57;3.00

ASMR: Age-Standardized Mortality Rates; CI: Confidence Interval *Significant change

According to the Joinpoint Regression Analysis, a statistically significant increase in deaths from breast cancer was observed during this period (AAPC:1.78 (CI: 0.57:3.00) p=0.009). When evaluated by regions, significant increases were observed in the TR2 region until 2013, in the TR5 region until 2012, and in the TRC region until 2017. Non-significant decreases were observed for all three regions from these years until the end of the period (Table 2, Figure 2).

According to the age groups examined, significant increases were observed in all age groups in Turkey. When the determined age groups were examined according to the regions, it was seen that there were significant increases, especially in the 65 and over age groups, according to the results obtained. Breast cancer death rate in women is strongly associated with age, which is the highest in the elderly population (Table 3, Figure 3). There were decreases only in the 55 and over age group in the TR1 region, in the 45-54 age group in the TR8

region, in the 45-54 age group in the TR9 region, and in the 65-74 age group in the TR5 region, although they were not statistically significant.

Table 2. Annual rate of women breast cancer mortality between 2009-20019.

	AAPC(95% CI) (2009-2019)	Period I		Period II	
		Years	APC (95% CI)	Years	APC (95% CI)
Overall	1.78 (0.57;3.00) (p=0.009)				
TR1	-0.47 (-1.59;0.67) (p=0.372)				
TR2	3.61 (0.48;6.84) (p=0.023)	2009-2013	9.22 (0.5;18.65) (p=0.040)	2013-2019	0.03 (-3.12;3.28) (p=0.981)
TR3	1.65 (0.15;3.17) (p=0.034)				
TR4	1.37 (-0.36;3.14) (p=0.107)				
TR5	1.03 (-0.77;2.86) (p=0.263)	2009-2012	4.58 (-2.32;11.98) (p=0.016)	2012-2019	-0.45 (-1.75;0.86) (p=0.428)
TR6	1.95 (0.15;3.77) (p=0.037)				
TR7	4.14 (1.83;6.51) (p=0.003)				
TR8	1.13 (-0.39;2.68) (p=0.127)				
TR9	3.51 (2.56;4.47) (p<0.001)				
TRA	4.68 (0.86;8.63) (p=0.021)				
TRB	5.63 (2.43;8.93) (p=0.003)				
TRC	3.72 (-0.52;8.15) (p=0.086)	2009-2017	7.19 (4.94;9.49) (p<0.001)	2017-2019	-9.06 (-28.92;16.35) (p=0.382)

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change.

Table 3. Women breast cancer mortality rates (100,000) and average annual percentage change (AAPC), by age groups, in Turkey and region, 2009-2019.

Region	<45 years of age			45-54 years of age			55-64 years of age			65-74 years of age			>74 years of age		
	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC
TR1	4.70	5.05	0.73	19.53	23.98	2.07	32.64	31.94	-0.22	52.00	45.08	-1.42	95.88	88.11	-0.84
TR2	3.66	5.93	4.94	16.53	21.53	2.68	23.41	28.29	1.91	28.49	36.76	2.58	33.93	57.41	5.40*
TR3	4.16	4.51	0.82	15.18	18.26	1.87	20.84	24.33	1.56	17.04	21.33	2.27*	43.09	61.35	3.60*
TR4	4.99	5.41	0.81	18.06	20.50	1.27	26.15	31.52	1.89	35.29	40.41	1.36	45.57	63.51	3.38
TR5	3.97	4.84	2.01	16.00	18.87	1.66	24.49	26.60	0.83	34.98	34.92	-0.02	63.00	63.51	0.08
TR6	3.53	5.42	4.37*	16.53	17.83	0.76	22.18	25.19	1.28	25.84	33.67	2.68*	33.76	53.62	4.74*
TR7	3.43	5.13	4.09	13.03	18.42	3.52	15.64	24.71	4.68	18.58	30.25	5.00*	26.70	50.16	6.51*
TR8	3.76	4.57	1.97	16.82	13.56	-2.13	16.33	20.82	2.46	20.15	24.14	1.82	32.34	45.26	3.42
TR9	4.13	3.99	-0.34	14.55	18.23	2.28	14.30	19.11	2.94	15.86	27.28	5.57*	23.55	46.54	7.14*
TRA	2.85	4.28	4.14	8.72	21.63	9.51*	14.00	22.75	4.97	29.66	42.94	3.77	36.89	38.78	0.50
TRB	3.59	4.46	2.20	9.17	22.04	9.16*	13.37	23.40	5.76	14.07	26.12	6.38*	17.93	45.82	9.84*
TRC	3.40	4.81	3.55	10.19	16.91	5.19*	12.36	21.46	5.67	15.65	24.53	4.59*	19.31	36.85	6.67*
Turkey	4.00	4.90	2.05*	15.72	19.40	2.13*	21.84	26.06	1.78*	28.84	33.84	1.61*	44.49	58.48	2.77*
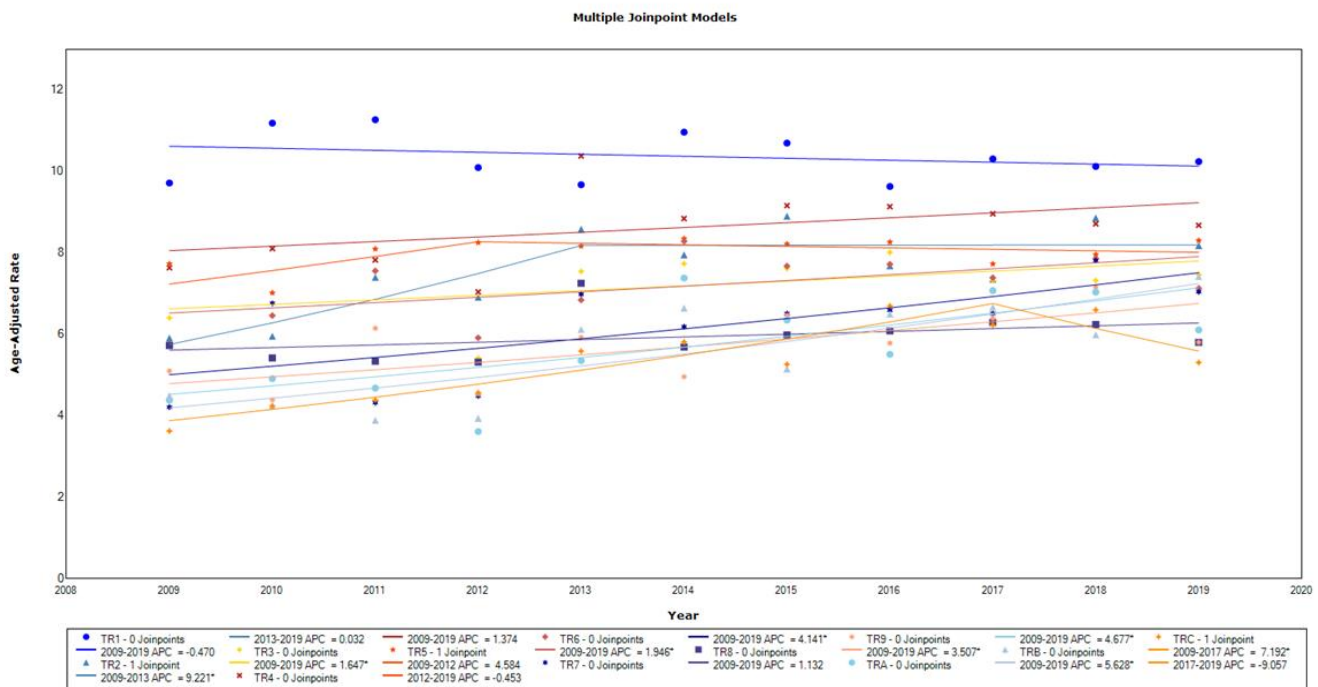
Figure 2. Trends in mortality from women breast cancer mortality in Turkey, results of JRA, 2009–2019
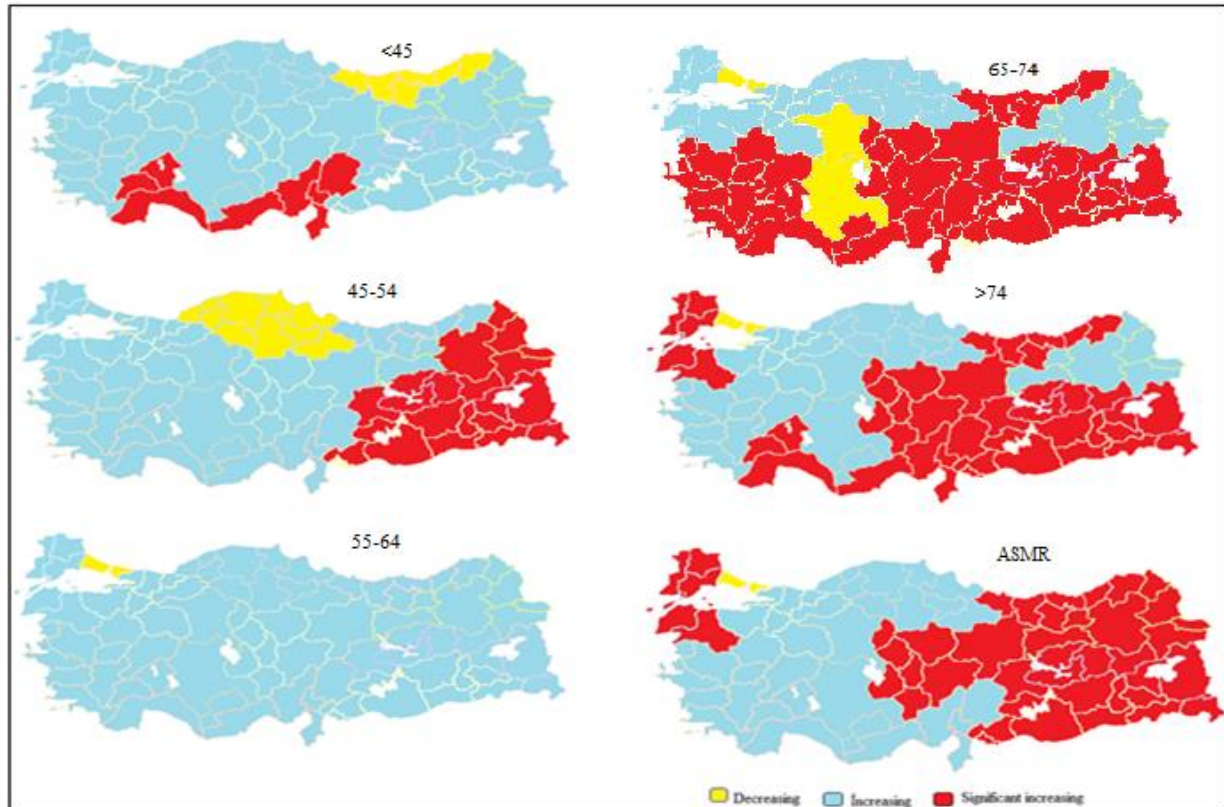
(ASMR: Age-standardized mortality rate.)

Figure 3. Trend of women breast cancer mortality, according to age group, for Turkey and its region, 2009-2019

Discussion

In this study, breast cancer mortality trends in women in Turkey and geographical regions from 2009 to 2019 were evaluated. The results show a significant annual increase of 1.78% in breast cancer-related deaths between 2009 and 2019. It has been observed that there are inequalities in breast cancer deaths by geographical regions. It was determined that the highest significant annual increase was in the Central Eastern Anatolia region, with 9.84%.

In contrast, Istanbul, one of 12 geographical regions with a decreasing trend in mortality rates, is located in the Western part of the country. This region has the lowest poverty rates and the highest oncological workforce compared to the eastern region. Therefore, easier and quicker access to health services and more opportunities to diagnose cancer in the population living in Istanbul may have a positive effect on early diagnosis of cancer.

Socioeconomic determinants that influence disparity in breast cancer mortality include poverty, culture, and social injustice. Poverty is a critical social factor driving health inequality.[12] Low-income women have significantly lower breast cancer screening rates, a higher probability of late diagnosis, and often receive inadequate and different treatment, resulting in higher death rates from breast cancer.[13]

It can be thought that the high mortality rates among people living in underdeveloped regions are associated with limited access to diagnosis and treatment opportunities and also the lower quality of health services and information about cancer. According to studies, breast cancer survival rates are lower in low- and middle-income countries due to such disparities, late diagnosis and poor access to cancer care compared to high-income countries. In high-income countries, successful screening programs and effective treatment and care have led to reductions in breast cancer-related deaths. Conversely, breast cancer-related deaths have increased in low- and middle-income countries.[14]

According to the results of a study covering European Union countries, the death rate due to breast cancer, which was 17.9 per hundred thousand in 2002, decreased to 15.2 per hundred thousand in 2012. The greatest regression was observed in the age group 49 years and younger. It was stated that early diagnosis, effective treatment methods and regular screenings reduce the deaths from breast cancer in Europe.[15]

In another study conducted in 24 EU countries, including the United Kingdom, it was stated that breast cancer deaths tend to decrease in all countries except Croatia, France and Poland.[16]

It is conceivable that the improvement in life expectancy in Istanbul may not be accompanied by healthier habits, access to health services and preventive medicine. Because the opportunities to access health services and information sources about health and economic standards are higher than in the eastern parts of the country, mortality rates tend to decrease in Istanbul.

The aim of cancer screening in our country is to reduce cancer-related deaths in the target population. Screenings are carried out free of charge in primary healthcare institutions, including Cancer Early Diagnosis, Screening and Training Centers (KETEM), Community Health Centers, Healthy Life Centers, Family Health Centers, and Mobile Cancer Screening Vehicles. KETEM enables the diagnosis and treatment of cancer in active stages by providing the importance of early diagnosis and public awareness. The breast cancer screening program for early detection of breast cancer in Turkey was started in 2012. The program includes the evaluation of women aged 40-69 with mammography every two years.[17.] Early diagnosis and screening both prevent deaths and improve the disease with simpler and cheaper treatments.

This screening practice tends to increase correct and early cancer diagnosis and consequently decreases death rates. Therefore, the higher mortality rate in the eastern regions and the higher mortality rate in older ages

may reflect the impact of the cancer screening program. However, it may be considered too early to see the benefits of this nationwide program to reduce mortality rates.

For community outreach, work has begun in areas such as educating Health supporters and ensuring patients adhere to their treatment regimens.

Family history is one of the most widely acknowledged risk factors for breast cancer. Breast cancer risk factors in families vary depending on the affected family members, their ages at diagnosis, and the number of unaffected women in the lineage. A woman is more likely to develop breast cancer if a first-degree relative has the disease when they are young or if they have multiple relatives who have the disease.[18] It can be thought that the high mortality rate in the eastern region of Turkey is due to genetic predisposition due to the high rate of consanguineous marriage, which is 4% in 2021, and most of them are in the East and Southeast parts of Turkey.[9]

In the breast cancer mortality rates in women in Turkey, a statistically significant increase was observed in seven regions (TR2, TR3, TR6, TR7, TR9, TRA, TRB) except TR1 in the 2009-2019 period, and non-significant increases were observed in other regions. The heterogeneity found in this study may be a reflection of economic factors, information sources about cancer, and changing situations to access health care for both early detection and adequate treatment.

Conclusion

In this study, regional differences in the breast cancer mortality trends over 11 years were found. Significant increases were observed during this period, especially in the eastern regions. When evaluated by age groups without regard to the geographical region, there are statistically significant increases in all age groups.

To our knowledge, this is the first study in Turkey to analyze breast cancer mortality trends by geographic region at the national level using JRA. Breast cancer is still a very important health problem in Turkish women of all ages. It is essential to take measures to reduce the breast cancer mortality rate and increase early diagnosis opportunities in our country.

Ethical Considerations: Ethics committee approval is not required for the study due to publicly available data has been used.

Conflict of Interest: The authors declare that they have no conflict of interest.

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