ARTICLE INFO

Received: 26 June 2018
Revised: 18 July 2018
Accepted: 24 July 2018

Key words: Breast cancer, Incidence, Mortality, Trends, Iran

ABSTRACT

Background: The present study aimed to investigate breast cancer trend, incidence, and mortality among Iranian women and was one of the first provincial and population-based studies to investigate breast cancer changes during 14 years in the largest province of Iran, Kerman.

Methods: This was a population-based longitudinal study. Information about women diagnosed with breast cancer from 2001 to 2014 was obtained from the Cancer Registry of Kerman University of Medical Sciences. Independent-samples t test, one-way analysis of variance, linear regression, time series graphs, and fitted line plots were performed using SPSS 22 and Minitab 17.

Results: A total of 2771 women were diagnosed with breast cancer in Kerman province from 2001 to 2014. The mean age of female patients was 49.52±12.88 years. The total incidence rate was 13.5 per 100,000 women and there was an increasing trend for incidence and age at diagnosis. Also, 254 women died from breast cancer during these 14 years and the mean mortality age was 54.16±14.33 years. There was also an increasing trend for mortality and age of death.

Conclusion: There is an increasing trend for incidence and mortality from breast cancer in Kerman province and this requires interventions such as appropriate screening programs. Also, enabling physicians and increasing patient awareness to identify breast cancer symptoms is necessary.

INTRODUCTION

Cancer, with 8.8 million deaths, was the second leading cause of mortality in 2015, as 1 out of 6 deaths in the world was caused by cancer.1 Approximately, 70% of cancer deaths occur in low- and middle-income countries,1 and cancer incidence and mortality is increasing in developing countries.2 Breast cancer is the second most common cancer worldwide,3 the most common cancer in women,4,5 and the leading cause of death from cancer in women.5 In 2015, 2.4 million new cases of breast cancer were diagnosed and 523 000 deaths from breast cancer were reported in the world.6 Although more than half of the global burden of breast cancer is currently from developed countries, its incidence is rapidly increasing in developing countries.7 Also, more than half of the deaths and about half of the new breast cancer cases occur in developing countries based on 2008 GLOBOCAN estimates.8
Breast cancer is also the most common cancer in Iranian women. It was the leading type of cancer in Iranian women, accounting for 24.6% of all cancers. The mean age of breast cancer diagnosis for Iranian women is 10 to 15 years lower than that for developed and Western countries. The mean age of diagnosis for American female breast cancer patients from 2008 to 2012 was 61 years. However, in Iran, most women diagnosed with breast cancer are younger than 50 years and most are diagnosed with invasive cancer at advanced stages.

Studies done in Iranian women showed that low levels of knowledge and insufficient awareness about breast cancer symptoms were among the most important factors causing delays in breast cancer diagnosis. Further studies in Iran showed that empowering women through education can increase early detection of breast cancer.

In developed and Western countries, such as the US, most deaths from breast cancer occur among women older than 50 years. In Iran, not only are deaths from breast cancer on the rise, but a large number of deaths happen among women younger than 50 years.

The present study aimed to investigate breast cancer trend, incidence, and mortality among Iranian women and was one of the first provincial and population-based studies to investigate the trends of breast cancer during 14 years in the largest province of Iran, Kerman.

Methods

This was a longitudinal and population-based study. Information about women diagnosed with breast cancer was inquired from the Cancer Registry of Kerman Province from 2001 to 2014. This study was approved by the Deputy of Research (No: 93/460) and Ethics Committee of Kerman University of Medical Sciences (No: K/93/636).

Variables including age at diagnosis, year of diagnosis, residential location, stage and grade at diagnosis, and status (being alive or not) were extracted. Hospital medical records were used to complete the information. Death dates were obtained from the Death Registration at Kerman University of Medical Sciences. Other unknown information was collected by contacting the patient or her family.

In order to estimate the annual incidence rates, the number of new breast cancer cases for each year was divided by the total number of females in the same year. National census data for 1996, 2006, and 2011 and population growth rates were used to calculate the female population of the province in each year.

Descriptive statistics, independent-samples t-test, one-way analysis of variance, linear regression, time series graphs, and fitted line plots were performed with Excel 2016, SPSS 22, and Minitab 17.

Results

Totally, 2771 women were diagnosed with breast cancer in Kerman province from 2001 to 2014. The mean and median ages at diagnosis were 49.52 ± 12.88 and 48 years, respectively. Also, 254 patients died of breast cancer during these 14 years, and the mean and median ages at death were 54.16 ± 14.33 years and 54 years, respectively.

Patients from rural areas (P < 0.001) and those with grade 3 at the time of diagnosis (P = 0.035), had a significantly lower age at diagnosis. Although the mean age of patients with stage III at diagnosis was also lower than the other stages, the difference was not statistically significant (Table 1).

The trend in age at diagnosis for female breast cancer patients in Kerman province during the 14 years is shown in Figure 1. As shown in the figure, the mean age at diagnosis did not show a significant trend (P = 0.16).

Table 1. Female Breast Cancer Patient's Characteristics in Kerman Province, Iran

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
<th>Age at diagnosis, Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>City</td>
<td>1677 (58.8)</td>
<td>49.92 ± 12.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rural</td>
<td>439 (15.4)</td>
<td>46.83 ± 12.37</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>735 (25.8)</td>
<td>50.25 ± 12.98</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2851 (100)</td>
<td>49.52 ± 12.87</td>
<td></td>
</tr>
<tr>
<td>Stage at diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>14 (0.5)</td>
<td>50.21 ± 16.52</td>
<td>0.132</td>
</tr>
<tr>
<td>I</td>
<td>135 (4.7)</td>
<td>48.73 ± 10.78</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>567 (19.9)</td>
<td>48.64 ± 11.30</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>395 (13.9)</td>
<td>47.94 ± 11.86</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>89 (3.1)</td>
<td>51.52 ± 13.42</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1651 (57.9)</td>
<td>50.17 ± 13.67</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2851 (100)</td>
<td>49.52 ± 12.89</td>
<td></td>
</tr>
<tr>
<td>Grade at diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>290 (10.2)</td>
<td>50.05 ± 12.89</td>
<td>0.035</td>
</tr>
<tr>
<td>2</td>
<td>893 (31.3)</td>
<td>50.01 ± 12.759</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>402 (14.1)</td>
<td>48.09 ± 12.72</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1266 (44.4)</td>
<td>49.51 ± 12.98</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2851 (100)</td>
<td>49.52 ± 12.87</td>
<td></td>
</tr>
</tbody>
</table>
The trend in breast cancer incidence in Kerman province from 2001 to 2014 is shown in Figure 2a. As shown in the figure, breast cancer incidence has been increasing in Kerman province ($P < 0.001$).

The forecast of breast cancer incidence in Kerman province up to 2020 is shown in Figure 2b. The best fit for the data was a third-degree model. If the incidence of breast cancer increases as predicted in Figure 2b, about 27 cases of breast cancer will happen per 100,000 females in Kerman province by 2020.
Figure 3 shows the mean age of death due to female breast cancer during the 7 years in urban and rural areas of Kerman province. The mean age of death among rural women was nonsignificantly lower than that of women living in cities ($P = 0.074$).

A large percentage of data was missing from 2001 to 2007 (91.9%), and because of this, data for these years were not included in Figures 4 and 5.

The trend in breast cancer mortality in Kerman province from 2008 to 2014 is shown in Figure 4. Breast cancer mortality did not show a significant trend during these 7 years ($P = 0.063$).

The trend in mortality age for female breast cancer patients in Kerman province from 2008 to 2014 is shown in Figure 5. The mean age of death due to breast cancer had an increasing trend from 2008 to 2014 ($P = 0.046$).
Discussion

The mean age at diagnosis for breast cancer was about 50 years among women in Kerman province. This age is lower in comparison with a developed country such as England, where the highest incidence of breast cancer happens after the age of 55.\textsuperscript{21} In the present study, the age-specific incidence rate was highest among women aged 40 to 55 years (46.22 per 100 000 females), and the median age of diagnosis was 48 years. However, according to the US National Cancer Institute, most women diagnosed with breast cancer in America were 55 to 64 years old and the median age of diagnosis of breast cancer was 62 years.\textsuperscript{22} Also, Mousavi et al., in a population-based study of the data from Tehran Cancer Registry in Iran from 1998 to 2001, showed that the mean age at diagnosis was 51 years and that although 36% of patients were aged under 40 years, the highest incidence rate was reported among women aged more than 60 years.\textsuperscript{23}

In the present study, the incidence rate for 2012 (17 per 100 000 females) was lower than the average standardized rate for the world (43 per 100 000 females) and Asian countries including Japan, South Korea (both 52 per 100 000 females) and Singapore (65 per 100 000 females).\textsuperscript{24}

The results of the present study showed that the age at diagnosis was significantly lower among women who lived in rural areas. In contrast, Mitchel et al, who studied breast cancer during 1999 in Australia, showed that there was no significant relationship between age at diagnosis and residential areas.\textsuperscript{25}

The incidence rates of breast cancer in the present study was 16.7 to 19.2 per 100 000 females from 2010 to 2014, and these results were lower than a developed country such as the USA, where the average incidence was 124.9 per 100 000 females from 2010 to 2014.\textsuperscript{21}

It seems that, compared with women in developed countries, Iranian women develop breast cancer at younger ages and visit doctors at more advanced stages of the disease. This needs more attention and appropriate screening programs.\textsuperscript{4}

Lifestyle and behavioral and nutritional habits are risk factors for many noncommunicable diseases and cancers, including breast cancer.\textsuperscript{26,27} In the last two decades, breast cancer has rapidly increased in the less developed regions of the world.\textsuperscript{3,4} Likewise, in the present study, breast cancer incidence showed an increasing trend, and this needs proper interventions including screening and periodical breast examinations.

A total of 1 426 (96.8%) BC cases undergoing mastectomy were pathologically staged. Of this number, 39.1% were stage III. The majority of cases were in stages III and IV combined (62.8%) (Figure 3). Only of 47 (3.2%) cases were residual cancers.

A total of 202 (13.7%) of the BC cases undergoing mastectomy were incompletely excised.

In the present study, although breast cancer mortality increased from 1 to 4.1 per 100 000 females from 2008 to 2014, that rate was still less than developed countries such as England and Wales.\textsuperscript{28} The mortality rate in England showed a decreasing trend from 2002 to 2006, but the adjusted mortality rate for different age groups was 30 per 100 000 females, which is much more than Iran.\textsuperscript{29} Also, according to the US National Cancer Institute, the mean breast cancer mortality rate in the US was 21.2 per 100 000 females from 2010 to 2014,\textsuperscript{30} while we found a breast cancer mortality rate of 1.9 to 4.1 per 100 000 females over the same period in Kerman province—although underestimations may have occurred due to low-quality data collection in Iran.

The results of the present study showed that although the mean age of death among women who lived in the rural areas was lower, this difference was not significant. In Europe in 2014, the mortality rate decreased by 9% compared with 2009,\textsuperscript{19} while, Taghavi et al. reported that breast cancer mortality had increased from 1995 to 2004 in Iran, with the increase being greater for women younger than 50 years.\textsuperscript{20} According to Rastad et al., lack of breast cancer awareness, not considering themselves at risk, fear of being diagnosed with cancer, and incorrect diagnosis and relief by physicians were among the most important factors for the delay in seeking treatment for breast cancer in Iran.\textsuperscript{18}

Considering the growing trend in breast cancer mortality and lower age of breast cancer death in Kerman province, as well as the results of previous studies,\textsuperscript{16} more appropriate measures should be taken to improve early diagnosis by enabling physicians and increasing patient awareness about breast cancer symptoms.

A limitation of this study was its missing data. About half of the cases had missing data on stage and grade.

In conclusion, breast cancer incidence is growing in Kerman province, and this needs appropriate interventions including screening, early detection, enabling physicians, and empowering patients to identify breast cancer symptoms. Also, providing greater access to facilities for early diagnosis and treatment of breast cancer patients in rural areas should also be considered.

Funding

This project was supported by Kerman University of Medical Sciences.

Conflict of interest

The authors have no conflict of interest.

Acknowledgment

The authors acknowledge Kerman University of Medical Sciences and Kerman Cancer Registry, especially Ms Sadeghi and Ms Rezaei for their
assistance with data collection.

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