Research Article

Breast Cancer in Central Iran: Estimated Incidence and Trend in Isfahan Province During 30 Years

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Abstract

Background: Breast cancer is not only one of the most common cancers in Iran, but is also a leading cause of cancer-related mortality in Iranian women. Evidence suggests that breast cancer occurs in Iranian women 10 years earlier than their peers in developed countries. To provide reliable estimates of the incidence and trend of breast cancer in central Iran, we conducted a cross-sectional study in Isfahan Province.

Methods: We calculated the incidence and trend of breast cancer during 1980-2010 in Isfahan Province, as the most populous metropolitan city in central Iran. We conducted this cross-sectional study in four major screening mammography centers during 2012-2014 to collect data regarding the patients' breast disease history. The final study sample consisted of 7883 women, 1275 of whom were diagnosed with breast cancer. Next, a retrospective cohort analysis was conducted on patients with breast cancer. Crude and age-standardized incidence rates (ASIR) were also calculated.

Results: During 2005-2010, ASIR was measured to be 40.4 per 100,000 person-years. The mean age of patients at the time of breast cancer diagnosis was 43.5 years (SD=8.2). The findings showed that the incidence rate of breast cancer increased steadily from 8.3 to 40.4 per 100,000 person-years from 1980 to 2010.

Conclusion: A significant increase was observed in the incidence of breast cancer, and a younger age of onset was reported in a major province over the past three decades.

Keywords: Breast Cancer; ASIR; Years of Life Lost (YLL)

Introduction

For decades, breast cancer has been the most common cancer among women. It is recognized as the leading cause of cancer-related mortality in developing countries and the second cause of mortality in developed countries [1-4]. According to previous reports, 1.7 million women were diagnosed with breast cancer in 2012. Over the past five years, nearly 6.3 million women have been diagnosed with this disease [1,3]. In 2013, breast cancer was ranked the fifth leading cause of years of life lost (YLL) due to premature death from cancer.

The steadily increasing incidence and prevalence of breast cancer, besides its substantial burden and significant cost of treatment, have made this disease one of the most important health concerns in every country [1,2,5,6]. Despite the lower incidence of breast cancer in developing countries, its prevalence in women is increasing more rapidly than developed countries. According to previous reports, the age-standardized incidence rate (ASIR) per 100,000 persons-year increased from 27.74 to 40.40 (46%) during 1990-2013 in developing countries. Also, the incidence rate rose from 69.75 to 74.98 (8%) in developed countries, with a global rise from 44.36 to 51.73 (17%) [1,3].

In Iran, as a developing country in Central Asia, breast cancer is recognized as the most common cancer and the most important cause of cancer-related mortality among women [7]. According to the most recent cancer registry by the Iranian Ministry of Health, the crude incidence rate of breast cancer in women was 22 per 100,000 in 2009 [8]. Although this rate is much lower than recent reports from developed countries or even some developing countries, it represents an increasing trend among Iranian women, compared to the incidence rates reported between 1965 and 2000 [7,8].

One of the greatest health concerns is that breast cancer occurs in Iranian women at least 10 years earlier than their peers in developed countries. The highest incidence of breast cancer has been reported in the age group of 40-49 years [9]. Also, the majority of these women are referred for diagnosis and treatment at advanced stages of their disease (TNM stage III or IV) [8,10-14]. Therefore, the actual burden of breast cancer in Iran may be higher than previously assumed [5].

Population-based studies on breast cancer incidence in Iran were neglected for almost thirty years [15]. Consequently, in the 21st century, cancer epidemiologists and other researchers have made concerted efforts in Iran to accurately determine the incidence rates and trends of breast cancer. Nevertheless, these efforts have been frustrated by the absence of a national cancer registry system and few, if any, prospective cohort studies as a reference for evaluating the true incidence rate instead of prevalence. In addition, the overall crude incidence rate of breast cancer per 100,000 person-years indicates significant discrepancies [16], with rates ranging from 17.1 during 1996-2000 [17] to 35.9 during 2003-2008 [16].

In an effort to provide reliable estimates of the occurrence and trend of breast cancer in Iran over the past three decades, we attempted to conduct a study in Isfahan Province, Iran. According to a national census in Iran in 2011, Iran has a population of nearly 80 million. Isfahan, with over three million inhabitants, is the third most populous city in Iran [18]. This city ideally represents the population of central Iran and indicates its racial and age structure, as well as breast cancer risk factors related to the environment and lifestyle.

According to previous breast cancer estimates based on Besag-York-Mollie (BYM) model (a standard model for estimation of ecological associations), women in Isfahan had a relative breast cancer risk of 1.38 during 2004-2008, which is only second to the capital (Tehran) [7,19]. In the present study, we aimed to precisely determine the incidence of breast cancer during 1980-2010 in Isfahan city, Iran.

Materials and Methods
Study population

The study was approved by the ethics committee of the Isfahan University of Medical Sciences prior to the initiation of the study. Women who were referred to one of the four main mammographic screening centers in Isfahan Province between January 2012 and February 2014, whether for diagnostic or screening purposes, were approached for informed consent at the time of mammography. These are the main cancer centers in the province and the majority of the cancer patients are referred to one of these centers during the course of their treatment. A final sample size of 7893 people was enrolled in the study after obtaining informed consents (nearly 80% of all eligible women). A questionnaire-based survey was conducted by the expert staff. Questions were read to the participants, and their answers were recorded.

Questionnaire and variables

The questionnaire used in this study consisted of two sections. The general section included questions about the baseline demographic characteristics, as well as the patient's obstetric history, breast disease, medication use, and family history of breast disease. Anthropometric measurements were performed by trained

technicians. Previous mammogram results were collected from the patients' electronic medical records (EMR), according to the Breast Imaging Reporting and Database System (BI-RADS) (data not shown in this article) [20]. Other information was primarily provided by the patients and confirmed using EMR to reduce the effect of recall bias. The second section of the questionnaire was only completed for patients who had a pathology-proven history of breast malignancy. This section contained questions about the patient's age at the onset of malignancy, tumor grade, tumor stage, tumor markers, and treatment regimen; only EMR was used to collect the data.

Secondary assessment of patients with breast cancer

A retrospective study was conducted for the 1275 participants who were diagnosed with breast cancer. These patients were diagnosed with breast cancer between 1980 and 2010 [21]. A manual search was performed by utilizing the concurrently emerging National Cancer Registry Database and pathology reports to verify the records of patients. Data search was conducted by using patients' first and last names, date of birth, and medical record number. For each patient, the initial year of breast cancer diagnosis (based on their pathology report or the oncologist note), stage, grade, tumor biomarkers, and treatment course (not reported in this manuscript) were extracted. For those with a discrepancy in the time of onset of breast cancer between the pathology and the physician's report, the pathology report was selected. Eighty-four patients were excluded from the study due to incomplete profiles and inability to confirm the initial date of their breast cancer diagnosis either from the pathology or the oncologist's report.

Data analysis

We conducted a series of cross-sectional and retrospective cohort analyses for this study. To standardize our findings, we used the direct method of standardization and the World Health Organization (WHO) standard population (2000) as our reference population. SPSS version 22 (SPSS Inc., Chicago, IL, USA) was used to calculate the person-years of life for the population at risk. Crude rate was calculated by dividing the number of new breast cancer cases in a specific year by the estimated mid-year population of women in Isfahan province in the same year by using national cen-

Characteristics	Total participants	Malignant cases	Non-Malignant cases	P value*
Number of cases	7809	1191 (15.2%)	6618 (84.8%)	-
Age (Mean ± SD)	49.5 ± 8.9	48.3 ± 8.2	56.2 ± 9.5	<0.001
Positive family history of breast cancer (First degree)	680 (8.7%)	108 (9.1%)	457 (6.9%)	<0.005
Parity (Mean ± SD)	3.29 ± 1.71	3.01 ± 1.65	3.35 ± 1.71	<0.05
Abortion	1398 (17.6%)	187 (15.7%)	1191 (18%)	0.2
Still Birth	468 (6%)	68 (5.7%)	404 (6.1%)	0.07
Menopause status				<0.001
Pre menopause	4271 (54.7%)	349 (29.3%)	3931 (59.4%)	
Post menopause	3537 (45.3%)	842 (70.7%)	2687 (40.6%)	
History of hormonal contraceptive usage	5326 (68.2%)	812 (68.2%)	4513 (68.2%)	0.1
History of HRT[3] usage	1000 (12.8%)	180 (15.1%)	788 (11.9%)	0.005
Breast feeding duration (Mean months ± SD)	55.6 ± 36	51 ± 41	59.6 ± 37	0.01
Smoking	219 (2.8%)	46 (3.9%)	159 (2.4%)	0.001
Alcohol consumption	31 (0.4%)	5 (0.4%)	26 (0.4%)	0.09
BMI (Mean ± SD)	27.76 ± 3.4	27.44 ± 3.2	28.11 ± 4.0	0.06

Table 1: Patients' baseline demographic features and their comparison between the malignant and non-malignant groups.

Age Group	Cases			World population*	Crude rate (per 100,000)	ASIR (per 100,000)
	Number	%	Person-year			
25-29	1	0	967.998	79272.2	103.3	81.9
30-34	3	0.2	5308	76073.3	56.5	43.0
35-39	34	2.8	19077	71474.9	178.2	127.4
40-44	75	6.2	71429.9	65876.9	105	69.2
45-49	175	14.69	81456.3	60378.8	215	129.7
50-54	257	21.57	80561.9	53681.2	319	171.2
55-59	231	19.39	48059.9	45484.1	481	218.6
≥ 60	415	34.84	64380.9	37187	645	239.7
Overall	1191	100	-	-	320.6	189.1

Table 2: Number, percentage, crude and age-standardized incidence rate (ASIR) of breast cancer in different age groups of women.
*WHO standard population of year 2000.

sus data, multiplied by 100,000 (18). The results are presented as age-specific (crude) and age-standardized incidence rates (ASIR) per 100,000 person-years [9].

Results

The patients' baseline demographic characteristics are presented in Table 1. Initially, the study sample consisted of 7883 participants, 6618 of whom had no history of breast cancer; also, 1275 participants had a documented history of breast cancer. After

Figure 1: The increasing trend of crude rate and age standardized incidence rate of breast cancer among different age groups of participants.

Figure 2: Three decades consistent increase in age-standardized incidence rate (ASIR) trends for breast cancer among participants: from 1980 to 2010 breast cancer incidence in Isfahan province has increased from 8.3 to 40.4 100000/year. AAPR during consecutive periods of 5 years, as well as the whole period is also depicted. AAPR during these 3 decades was 1.07%.

* Average Annual Percentage Rate.

excluding 84 malignant cases due to incomplete profiles, the total number of patients was 7809 (1191 malignant cases). During the study, the mean age of followed-up malignant patients was 48.3 years (SD=8.2). On the other hand, the mean age of patients at the time of breast cancer diagnosis was 43.5 years (SD=8.2). As presented in Table 2, the overall crude incidence and ASIR of breast cancer were 320.6 and 189.1 per 100,000 person-years, respectively between 1980 and 2010.

Figure 1 indicates an increase in breast cancer trends by age with respect to the crude incidence rate and ASIR of breast cancer at the time of inclusion in the study. The highest incidence rate of breast cancer was reported in women aged ≥60 years, followed by women in the age ranges of 55-59 and 50-54 years, respectively.

Figure 2 shows a steady increase in ASIR over three decades. The incidence rate of breast cancer increased from 8.3 in 1980 to

40.4 in 2010 per 100,000 person-years. The average annual percentage change (AAPR) was 1.07% in this period.

Discussion

Based on our findings, ASIR of breast cancer was 40.4 per 100,000 from 2005 to 2010. Furthermore, our results showed that the incidence of breast cancer has increased steadily from 8.3 to 40.0 per 100,000 over the past three decades. These results are consistent with the findings reported in other countries, including the Middle East and North Africa (35.75), Central Asia (44.9), Iraq (55.71), Turkey (42.24), and Egypt (37.13) per 100,000 people. However, these rates are much lower than those reported from North American and Western European countries (111.01 and 82.04 per 100,000, respectively) [1].

Earlier studies from Iran indicated a lower incidence of breast cancer, with rates ranging from 17.1 during 1996-2000 to 22.4 in

1998 [7,10,17]. However, more recent studies, including the one conducted in 2006 in Fars Province (30.36) [22] and the one performed in East Azerbaijan Province (35.9) between 2003 and 2008 [16], indicate the higher incidence of breast cancer, similar to the present study. The majority of epidemiological studies on breast cancer have reported a similar pattern [2,16,23,24]. The increased incidence rate may be partly attributed to improvements in breast cancer screening techniques and programs, increased participation of women in screening programs, and improvement of data registry systems for breast cancer, particularly in developing countries, such as Iran [25-27]. Also, in the past few decades, adoption of a high-fat diet by Iranians (associated with a concomitant increase in BMI), decreased parity and breastfeeding duration, increased age of first pregnancy, and hormone replacement therapy are likely to play important roles in the increased incidence of breast cancer [9,28,29].

Our study, which was conducted between 2012 and 2014, showed that the mean age of participants at the time of breast cancer diagnosis was 43.5 years (SD=8.2), and 65.16% of these women were under 60 years. This rate is slightly lower than the rates reported in other Iranian and Asian studies published between 2000 and 2011, which reported that the mean age of patients was nearly 45 years at the time of diagnosis [15,21,31]. Nevertheless, our study, similar to earlier Iranian and Asian reports, revealed that breast cancer occurs in Iranian women 10 years earlier than their peers in developed countries [12,17,30]. This important difference in age at the onset of a major disease has been attributed to the younger population structure of developing countries or higher number of younger women participating in breast cancer screening programs [30]. However, adjustment of previously reported results for age, in addition to the assessment of age at the time of diagnosis in the first and second generations of immigrants from developing to developed countries [10,12,23], did not support this view.

Age of disease onset is likely to depend on a variety of factors, such as tumor biology (e.g., estrogen receptors, progesterone receptors, and HER2/neu status), breast density, and genetic factors, all of which may have different effects in developing and developed counties [12,20,25]. In developing countries, the lower registration rate of breast cancer in elderly patients has been the subject of some speculations [12]. Therefore, future studies are urgently needed to explore factors, leading to the earlier age of breast cancer onset in the Middle East and Asia and its increasing prevalence.

In our study, the highest incidence rate of breast cancer was reported in women aged 60 years or above, followed by women in the age ranges of 55-59 and 50-54 years, respectively. Comparison of breast cancer incidence by decade of life indicated the highest incidence in the fifth decade of life in patients. This finding is in contrast to some earlier studies in Iran, which reported the highest incidence of breast cancer at the age of 40-49 years [10,17]. This discrepancy may be due to the increased participation of older Iranian women in breast cancer screening programs and improved data registry systems for breast cancer in Iran [10,30].

Conclusion

The results showed a significant increase in the incidence of breast cancer in Isfahan over the past three decades and indicated

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