

Prevalence and Incidence of premenopausal and postmenopausal breast cancer in Iran in 2010

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ABSTRACT

Background: We studied the patterns of premenopausal and postmenopausal breast cancer incidence and its established risk factors in Iran in 2010. In addition, we estimated the 5-year prevalence of breast cancer in the country.

Methods: We performed an internet and library literature review. We used national cancer registry data, demographic health surveys, national censuses and World Bank data in this study. We used incidence rate and weighted survival rate of breast cancer and estimated five-year prevalence of breast cancer in Iran.

Results: Incidence rate of postmenopausal breast cancer varied significantly within country. The highest ASR was in Tehran province and reached 164.1 Per 100000 and the lowest ASR (13.9/100000) belonged to Sistan & Baluchistan. We found significant inverse correlation between postmenopausal breast cancer incidence and family size ($r=-0.579$, $p=0.001$), illiteracy ratio ($r=-0.703$, $p<0.0001$), and direct correlation for urbanization ratio ($r=0.554$, $p=0.002$) and life expectancy ($r=0.659$, $p<0.0001$). However one to six month breastfeeding was not significantly correlated with postmenopausal breast cancer incidence. Adjusting for the 15% underestimation in the pathology based cancer registry, the estimated number of new breast cancer was about 10,000 and the five-year prevalence was about 40,000.

Conclusion: Postmenopausal breast cancer is increasing in Iran. We suggest planning for the primary prevention and cost-effective early detection program for breast cancer in Iran, particularly for postmenopausal breast cancer which is going to be the main burden in the near future.

Keywords: Breast cancer, Incidence, Prevalence, Epidemiology, Iran.

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Introduction

There were about 1.4 million cases of breast cancer worldwide in woman in 2008 and it is the leading cause of death among woman in the world.¹ While incidence and mortality rate of most cancers including female breast cancer is decreasing in the USA and most European countries, it has been increasing in less developed countries because of transitioning to western life styled.¹⁻³ There is about more than 4 folds differences in the age standardized incidence rate (ASR) of breast cancer across the world, varying from 19.3 per 100,000 women in Eastern Africa to 89.9 per 100,000 women in Western Europe. It is estimated to be more than 80 per 100,000 in the more developed regions of the world (except Japan) and less than 40 per 100,000 in the less developed.¹

According to the Iranian cancer registry, ASR of breast cancer was 28.25 per 100,000 in 2009. However, there was up to 8-folds differences in the ASRs within country, ranging from, and 49.78 per 100000 in Tehran to 5.67 per 100,000 in Sistan & Baluchistan provinces.⁴

Majority of geographical variation in risk of breast cancer was linked to the differences in the environmental exposures such as reproductive factors, hormonal factors and socioeconomic status.^{3, 5-7} In addition, studies indicate that early age of first birth, high parity, breast feeding for 1 to 2 years can explain the large differences in breast cancer incidence between developed and developing countries.⁸

Some case-control studies reported that higher education, late menopause, history of induced abortion, overweight and obesity, positive family history of breast cancer, and OCP use⁹⁻¹² were associated with the risk of postmenopausal breast cancer among Iranian women. Furthermore, having more episodes of full term pregnancy, longer duration of breast feeding, lower age at first birth and parity were shown to be protective factors.^{9-11, 13} However, the reason behind the large variation and its association with these risk factors is not explained yet.

In this study, we evaluated the incidence and prevalence of breast cancer and its geographical pattern in Iran. We further studied the association of the observed pattern with the distribution of the established risk factors for breast cancer. The results of this study shed further light on the etiology of breast cancer in Iran. In addition,

it provides informative data for policy making and cancer control planning.

Method

This was a cross sectional study. In order to conduct this study, we used national cancer registry data and studied the incidence rate, prevalence and geographical pattern of breast cancer incidence in Iran. In addition, we used data from the national census, the demographic health surveys to investigate temporal trends of the established risk factors of breast cancer and their correlation with the incidence pattern of postmenopausal breast cancer. In addition, we used World Bank data and obtained information about total fertility rate and life expectancy in Iran. In addition, we used survival rate of breast cancer from the published literature to estimate the prevalence of the breast cancer.

National Cancer Registry

Although Shiraz and North of Iran cancer registries were established before 1979 but the first report of cancer registry in Iran was published in 1986, when it was pathology-based and reported the cancer incidence only based on the pathology reports.⁴ The pathology-based cancer registry was continued until 2007. Afterwards national cancer office improved the cancer registry and launched the population-based cancer registry in some selected provinces including Ardabil, Isfahan, Tehran, Khorasan Razavi, Khuzestan, Semnan, Fars, Kurdistan, Kerman, Golestan, Gilan, Lorestan, Mazandaran, Hamedan and Yazd. In the population-based cancer registry, additional data was collected from the death registry, clinics/hospitals, etc. The first report of the population-based cancer registry which reported the cancer statistics for 2008 was published in 2012.⁴

We obtained breast cancer incidence data from Iranian national cancer registry for the year 2009. The report was based on ICD-10 classification and we used codes C50 and D05 included both malignant neoplasm and carcinoma in situ of breast in our analyses.

Demographic Health Surveys (DHS) and National Censuses

We linked incidence data to Iran census 2006 (urban-

ization ratio, Life Expectancy) and Iran DHS 2000 (Illiteracy ratio, Family Size, Breastfeeding 6 Month) data to evaluate the underlying reason for the different distribution of the breast cancer incidence across the country.

National Census had been conducted every ten years from 1956 to 2006 in Iran, but the last round was in 2011. The survey studied characteristic, size and structure of the Iranian population. DHS were conducted in 2000 and 2010 and provide data on a wide range of health indicators including household sanitary and welfare facilities, social and health indicators, fertility and birth in women, family planning and contraception and child health and welfare.

Review of the literature on breast cancer survival rate

We searched English language literature published between 1990 and 2012 through Pubmed, Embase and Google scholar databases. The medical subject headings (MeSh) were "breast cancer" and "breast neoplasm", combined with "survival" AND "Iran". In addition, we looked for the papers published in the Farsi language in the Persian medical literatures using Iran Medex, Magiran, Scientific Information Systems (SID) and Iranian Medical Library (MEDLIB) with similar strategy, using Persian keywords equivalent to their English words. Studies were evaluated qualitatively through expert opinions. We eliminated studies that have been done in specific group of patients duplicate publication published in both in Persian and English languages, and the ones which did not report survival rates.

Statistical Analyses

We graphed the ASR of breast cancer in overall for all 30 provinces. We used age 50 years to stratify the breast cancers to premenopausal and postmenopausal breast

cancer. We used spearman correlation coefficient to determining the association of the distribution of ASRs above 50 years and established risk factors across country. Furthermore, we used the census data from 1956 to 2010 and studied the temporal trends for all established risk factors including literacy ratio, urbanization ratio, mean age of marriage and family size. Data on life expectancy and total fertility rate were extracted from World Bank Data for 1966 to 2010. We considered urbanization ratio, life expectancy and literacy ratio as the proxies for socioeconomic status. Total fertility rate, mean age of marriage, family size and breastfeeding were used as the measures for reproductive status.

We used the incidence rate of breast cancer and survival rates to estimate five-year prevalence of breast cancer in 2010. Survival rates were estimated from the result of our systematic review where we estimated average of the one to five years survival rates which were weighted by the sample size of the reported studies.¹⁴⁻²³ we used the data of the national cancer registry for the incidence rate of breast cancer. Following formula was used for the estimation of the prevalence of breast cancer Iran.²⁴

$$P_k = \sum_{i=1}^n IC_{k-i} \times S_{k-i}(i - 0.5)$$

Where "P" stands for prevalence number, "n" for the number of years for which we estimated the prevalence (1 to 5 years), "IC" for the number of breast cancer occurred in each year (incidence number) and "S" indicates survival rate for different follow-up time periods at the mid-year (from one to five-year). The estimation method was graphically illustrated in **Figure 1**.

Because, it was reported that the incidence rate of breast cancer was underestimated about 15% in the Iranian national cancer registry,²⁵ we adjusted the incidence

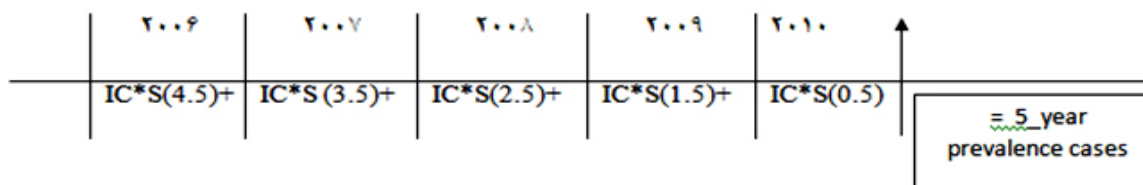


Figure1. Schema illustrating the formula for calculation of 5-year prevalent cases. IC indicates incidence cases number, S proportion of cases surviving t years. source:Pisani P etal:2009.

rate of breast cancer for this underestimation before using in the formula. Because, population-based cancer registration was started recently and previous data was only based on pathology-based cancer registry, we were not able to estimate actual annual percent change (APC) of breast cancer incidence in Iran. However, we reviewed the literature from other countries to estimate incidence rate of breast cancer for the previous years from 2006 to 2010. According to Scarlett Lin Gomez et al study APC of breast cancer incidence in Asian- Americans varied from 1.2 in Chinese to 4.7 in Korean citizens between 1990 and 2008 and about 3 for Indian/Pakistani citizens.²⁶ So we considered low (APC=1.2), medium (APC=3) and high (APC=4.7) scenarios to estimate incidence rate for years before and after 2009.

All statistical tests were two-sided, and P-values less than .05 were considered statistically significant. Statistical analyses were performed using excel 2007 and SPSS 20. We used ArcGIS 10 to graph the distribution of breast cancer incidence rate in the country.

Results

We found that 8810 breast cancer cases were diagnosed in Iran in 2009. The highest ASR of incidence were observed in Tehran province (49.8 per 100000) followed by Isfahan (40.9 per 100000), Yazd (40.0 per 100,000), Markazi (38.6 per 100000 and Fars (37.1 per 100000) provinces. In contrast, ASRs of breast cancer were considerably low in Sistan&Baluchistan (5.67 per 100000), Hormozgan (12.4 per 100000), Zanjan (12.9 per 100000),

Qom (13.2 per 100000), Ardabil (13.4 per 100000) and Illam (13.8 per 100000) provinces (Figure 2). Analysis by age showed that ASR of premenopausal breast cancers was equivocally low among all provinces, although the ASRs of the postmenopausal breast cancer varied across the country. ASR of the postmenopausal breast cancer was 164.1 per 100000 in Tehran province which was about 12-folds higher than the incidence rate in Sistan&Baluchistan (ASR=13.9). The ratio of the postmenopausal to premenopausal breast cancer was 14.18 on average (Figure 3).

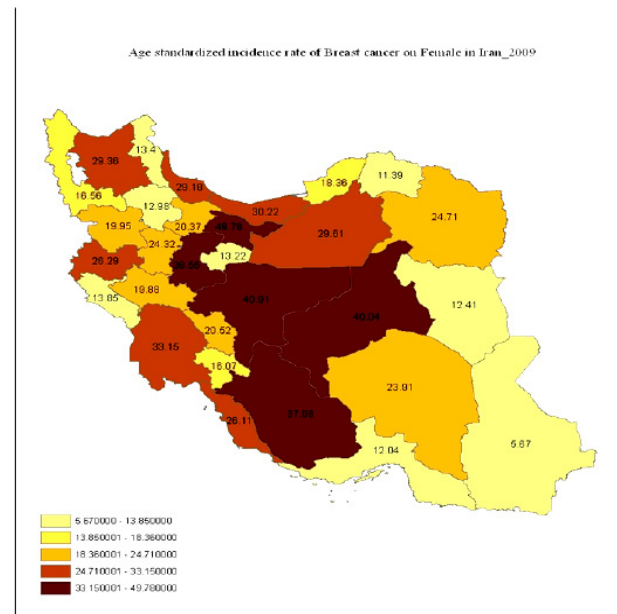


Figure 2. Age standardized incidence rate of breast cancer by province, Iran; 2009

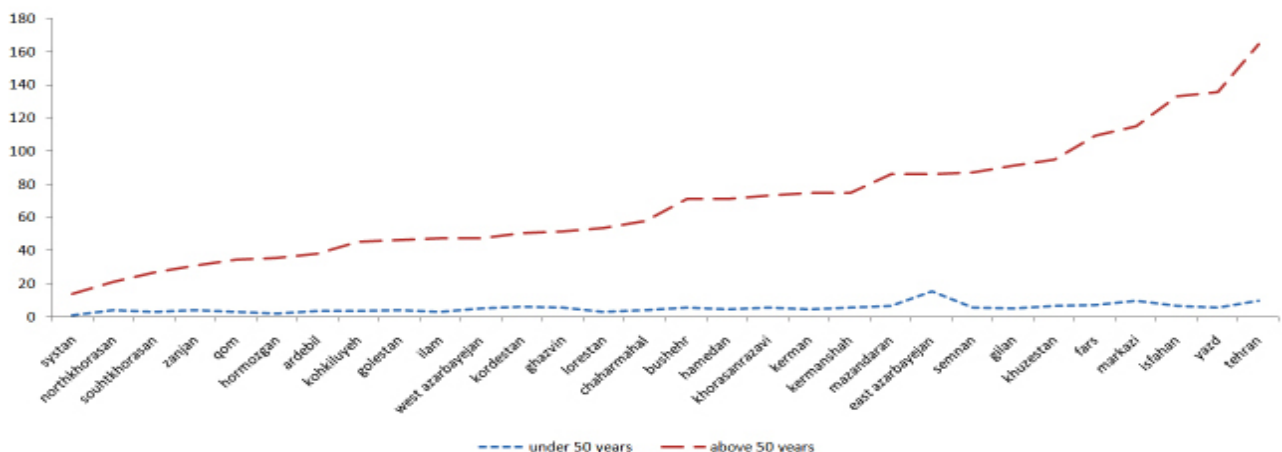


Figure 3. Comparison of ASR under and above 50 years by province, Iran; 2009

Postmenopausal breast cancer incidence was significantly correlated with family size ($r=-0.609$, $p=0.001$), illiteracy ratio ($r=-0.734$, $p<0.0001$), urbanization ratio ($r=0.548$, $p=0.003$) and life expectancy ($r=0.683$, $p<0.0001$) (Table 1). However, we found no statistically significant correlation between postmenopausal breast cancer incidence and one to six month breastfeeding.

Temporal trend of established risk factors of breast cancer are presented in Figure 4. Literacy ratio, urbanization ratio, means age of marriage and life expectancy had increased over time from 1956 to 2010. Literacy ratio increased from 8 to 81.1 percent and life expectancy from 48.81 to 74.669 years. In contrast, family size decreased at the same time period. Moreover, total fertility rate decreased from 6.7 to 1.67 births per woman.

Estimating breast cancer prevalence Only 16 Studies out of 20 were eligible and their survival rate were included. After adjustment for the 15% underestimation in the pathology based cancer registry, we estimated that number of new breast cancer 9656, 9827, 9990 and the five year prevalence was 40240, 39634 and 39079 for the low, medium and high APC scenarios, respectively (Table 2).

Discussion

In this study we found that the incidence rate of postmenopausal breast cancer was not distributed evenly across the country. It was higher mostly among big and industrialized cities. In addition, the result of the study showed that family size, illiteracy ratio, urbanization ra-

Table 1. Spearman Rank Correlation Coefficients between the ASR above 50 years 2009 and Representative Risk Factors.

Parameter	r	p-value
Urbanization ratio	0.554	0.002
Life expectancy	0.659	<0.0001
Family size	-0.579	0.001
Breastfeeding 6 month	-0.102	0.604
Illiteracy ratio	-0.703	<0.0001

tio and life expectancy has significantly direct association with increased incidence of postmenopausal breast cancer in Iran. Reviewing the temporal trend of established risk factors in Iran indicates the increasing trend of literacy ratio, urbanization ratio, mean age of marriage and life expectancy and decreasing trend of family size and total fertility rate as factors influencing breast cancer incidence rise in Iran.

Breast cancer was the common cancer in woman for all provinces except Ardabil and Kohgiluyeh & Boyer-Ahmad. In Ardabil, stomach and esophagus cancer were the common cancers in woman and in Kohgiluyeh & Boyer-Ahmad Province skin melanoma cancer was the first one.⁴ However in developing provinces like Sistan & Baluchistan communicable diseases like TB²⁷ are the leading health problem than non-communicable diseases like cancer.⁴ Due to concentration of the hospitals and oncology center in the large and more developed cities, many of the patients are referred to these centers and may overestimate the cancer incidence rate in the more

Table 2. Estimation of breast cancer Prevalence cases on female in iran_2010.							
year	Estimated incidence cases			Survival rate (1 to 5 years)	Cumulative prevalence cases		
	Scenario 1* (APC=1.2)	Scenario 2** (APC=3)	Scenario 3*** (APC=4.7)		Scenario 1* (APC=1.2)	Scenario 2** (APC=3)	Scenario 3*** (APC=4.7)
2006	9202	8708	8258	0.70	6717	6357	6028
2007	9314	8977	8665	0.76	14108	13480	12904
2008	9427	9255	9093	0.81	22105	21332	20618
2009	9541	9541	9541	0.88	30816	30043	29329
2010	9656	9827	9990	0.95	40240	39634	39079

*Low annual percent change, **Medium annual percent change, ***High annual percent change

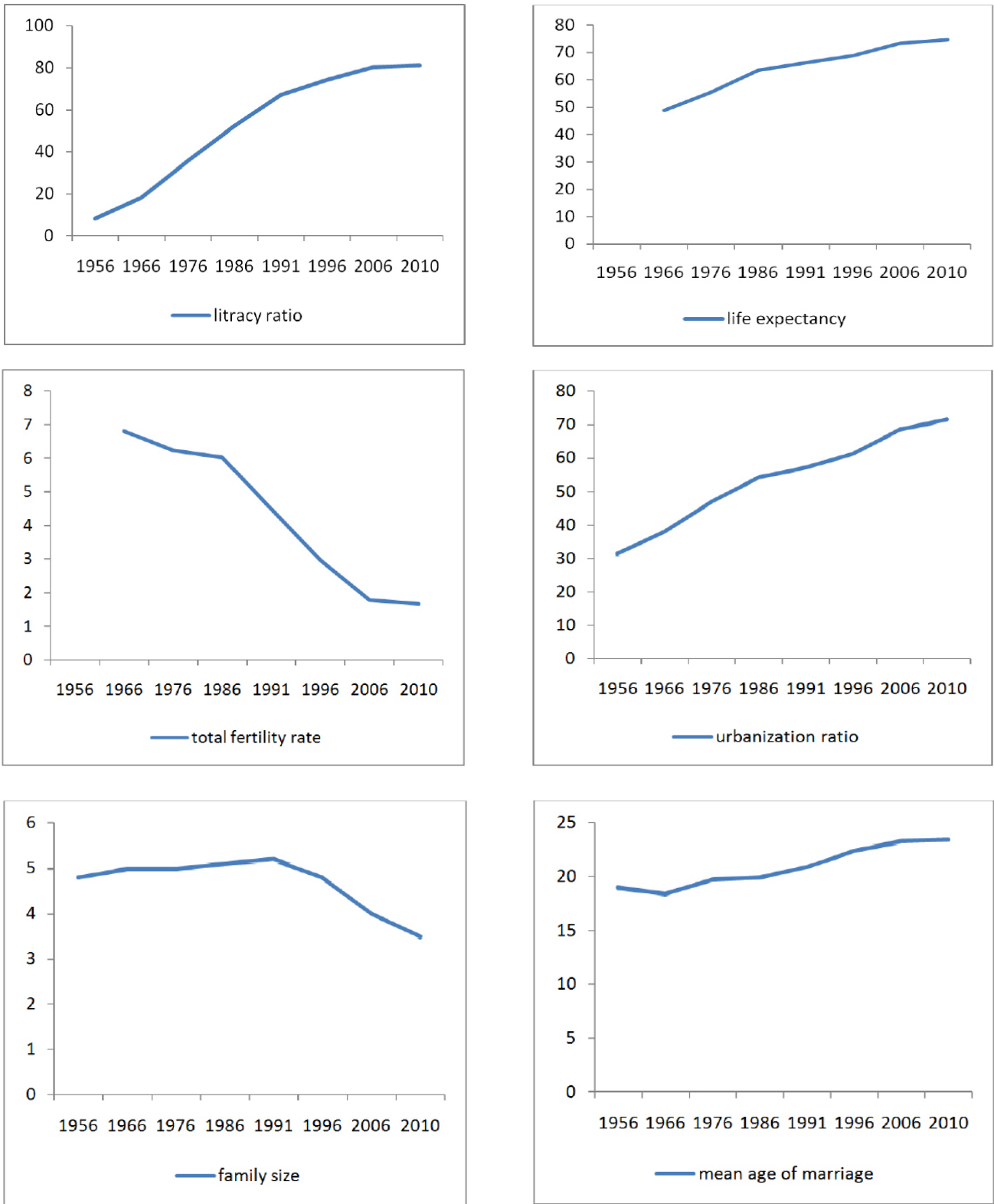


Figure 4. Temporal Trend of Representative Risk Factors, 1956-2010.

developed regions. This issue is considered in the national cancer registry and patient reports are returned to the cancer registry data of their residential area. A different result from the analyses of pre-menopausal breast cancer and homogenous distribution across the country was reassuring that this issue did not create major bias in this analysis.

Our results support the previous Studies that showed discrepancies in postmenopausal breast cancer are highly attributed to the extent of socioeconomic development and developed countries report higher incidence rate of postmenopausal breast cancer than the developing countries.⁸ Moreover our study shows that cities with higher urbanization ratio had higher incidence rate of postmenopausal breast cancer.

Increasing of life expectancy in developing countries, improvement in socioeconomic status, and reduction of communicable disease burden has leads to an increasing trend in the incidence rate of breast cancer in developing countries.²⁸ In the human development report 2013 human development index (HDI) was categorized to four categories including very high(0.905), high(0.758), medium(0.640) and low(0.466) HDI .Iran was one of the countries which has relatively highHDI(0.742) due to relatively high education and life expectancy.²⁹ Studies showed that incidence of breast cancer are higher in countries with higher HDI than countries with lower HDI.³⁰ Over the past decades, HDI has improved significantly all over the world and its pace of improvement has been fastest in low and medium human development categories.²⁹ Cancer statistics projections for 2030 revealed that cancer incidence will increase about 75% in 2030 compared to 2008. Share of this projection was about 69% in countries with high and very high HDI and about 81% in countries with low and middle HDI.³⁰

According to Boyle et al study, moving toward more civilized life styles leads to the later age of marriage, low parity, late age of the first birth and decreasing in breastfeeding duration that are known risk factors for postmenopausal breast cancer incidence.³¹ It is hypothesized that these changes are partly stemmed from women education. In this study we showed that the literacy ratio among women was higher in cities that had higher incidence rate of postmenopausal breast cancer. These findings indicate that the majority of the variation of breast

cancer in different regions of Iran is associated with the distribution of the known risk factors and higher occurrence of postmenopausal breast cancer in the more developed regions.

Reproductive factors are endogenous environmental exposures that are highly associated with postmenopausal breast cancer.^{32,33} In our study, cities with lower family size had higher incidence rate of breast cancer. We couldn't find a significant relationship between postmenopausal breast cancer incidence and distribution of breastfeeding in the country. Moreover other studies found no association between risk of postmenopausal breast cancer and breastfeeding.¹⁰ However the protective effect of breastfeeding is limited to premenopausal breast cancer which is relatively weak.³⁴⁻³⁶

In this study we estimated the 5-year prevalence of 40,000 for breast cancer in Iranian 2010. It seems that cancer prevalence rise rapidly in future years in Iran as a result of increasing trend of risk factors, aging of the population, higher detection rate of cancer and finally improvement in the breast cancer treatment. This data can be used to measure burden of breast cancer and highlight the importance of breast cancer in the health care system as well as resource allocation requirements to control programs.

Conclusion

Postmenopausal breast cancer is increasing in Iran. We suggest planning for the primary prevention and cost-effective early detection program for breast cancer in Iran. While standardization of the diagnostic and treatment approaches is necessary for both premenopausal and all postmenopausal breast cancer, it is important to prioritize the prevention of postmenopausal breast cancer which is going to be the main burden in the near future.

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