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Marked increase in breast cancer incidence in young women: A 10-year study from Northern Iran, 2004–2013

Abdolreza Fazel[a,b,1], Susan Hasanpour-Heidari[c,1], Fatemeh Salamat[a], Siamak Rajaie[a], Vahideh Kazeminezhad[a], Mohammad Naeimi-Tabiei[a], Ataollah Jahangirrad[d], SeyedMehdi Sedaghat[e], Reza Hosseinpoor[e], Fatemeh Ghasemi-Kebria[c], Gholamreza Roshandel[c,*], Elisabete Weiderpass[f,g,h,i]

[a] Cancer Research Center, Golestan University of Medical Sciences, Gorgan, Iran
[b] Omid Cancer Research Center, Omid Preventive and Health Promotion Center, Golestan University of Medical Sciences, Gorgan, Iran
[c] Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
[d] Department of Oncology, Laleh Hospital, Tehran, Iran
[e] Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[f] Department of Research, Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway
[g] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
[h] Genetic Epidemiology Group, Folkhälsan Research Center, Faculty of Medicine, Helsinki University, Helsinki, Finland
[i] Department of Community Medicine, University of Tromsø, The Arctic University of Norway, Tromsø, Norway

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ABSTRACT

Introduction: Breast cancer is the most frequent cancer among women worldwide. Breast cancer incidence in young women is a health issue of concern, especially in middle-income countries such as Iran. The aim of this study is to report the breast cancer incidence variations in Golestan province, Iran, over a 10-year period (2004–2013).

Methods: We analyzed data from the Golestan Population-based Cancer Registry (GPCR), which is a high-quality cancer registry collecting data on primary cancers based on standard protocols throughout the Golestan province. Age-standardized incidence rates (ASRs) and age-specific incidence rates per 100,000 person-years were calculated. Time trends in ASRs and age-specific rates were evaluated using Joinpoint regressions. The average annual percentage change (AAPC) with correspondence 95% confidence intervals (95%CIs) were calculated.

Results: A total of 2106 new breast cancer cases were diagnosed during the study period. Most cases occurred in women living in urban areas: 1449 cases (68%) versus 657 cases (31%) in rural areas. Statistically significant increasing trends were observed over the 10-year study period amongst women of all ages (AAPC = 4.4; 95%CI: 1.2–7.8) as well as amongst women in the age groups 20–29 years (AAPC = 10.0; 95%CI: 1.7–19.0) and 30–39 years (AAPC = 5.1; 95%CI: 1.4–9.0).

Conclusion: The incidence of breast cancer increased between 2004 and 2013 in Golestan province amongst all age groups, and in particular amongst women aged 20–39 years. Breast cancer should be considered a high priority for health policy making in our community.

1. Introduction

Today, cancer is one of the main causes of death worldwide after cardiovascular disease and stroke [1]. In 2018, breast cancer is estimated to be the most common type of cancer and the main cause of cancer death amongst women worldwide, with 2,088,849 million new cases and 626,679 deaths [2].

The incident rate of breast cancer is 46.3 per 100,000 worldwide [2], and the total number of breast cancer cases is predicted to increase in the future, reaching 3 million in 2030 [2,3].

Incidence rates are higher in high-income countries: North America, Western Europe and Oceania, as compared with Africa, South America and Asia [2]. The breast cancer screening program, as well as a higher prevalence of risk factors, explain the higher incidence in these

* Corresponding author at: Golestan Research Center of Gastroenterology and Hepatology, Sayyad Shirazi Hospital, Sayyad Shirazi Boulevard, Gorgan, Iran.
E-mail address: roshandel_md@yahoo.com (G. Roshandel).
[1] Equally contributed as first author.

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countries [2,4,5]. According to epidemiological studies, many risk factors have been proposed for this cancer, including genetic susceptibility, early menarche, lower parity, late age of having first child, shorter periods of breastfeeding, use of contraceptive and postmenopausal hormones, overweight and obesity after menopause, lack of physical activity, and consumption of alcohol [6–9].

Although the incidence of breast cancer in Asian women is lower than that in Western countries, recent reports suggest increasing trends (5% per year) in Asian and other developing countries [10–12]. In Iran, breast cancer is the most common of all cancer types; age standardized incidence rate is high (ASR = 31) (per 100,000 person-years) and is expected to rise (ASR > 70) by the end of 2030 [2,13]. Comparison studies between Western and Asian countries illustrate different patterns of breast cancer among female populations, including increasing trends of breast cancer among young women [12,14]. The peak of breast cancer in Iran occurred in women aged 40–49 years, in contrast to that in Western countries but similar to that in Asian countries, suggesting a high incidence of breast cancer in young Iranian women [3,15–18]. The recent report from the Golestan Population-based Cancer Registry (GPCR) showed a rapid increase in age-specific incidence rates of breast cancer among young women in the Golestan province of Northern Iran [19,20]. While the incidence of breast cancer in younger women (premenopausal) is lower than in elderly women (postmenopausal), their related risk factors are known to differ [21]. Thus, breast cancer will be a major health problem with a considerable burden on healthcare systems in middle-income countries such as Iran in the near future [15,22,23]. Studying the epidemiology of breast cancer and its risk factors will help health policy makers to design effective prevention and early detection programs [24]. Golestan province, located on the Asian esophageal cancer belt in Northern Iran, has been known as a high-risk area for esophageal cancer since the 1970s [25,26]. It consists of 14 counties, 33 cities and 1051 villages. In this study, we aimed to report 10-year incidence rates and epidemiological patterns of breast cancer, especially in young women in the Golestan province of Iran.

2. Materials and methods

Golestan has a population of about 2 million, representing about 2.3% of the total population of Iran. About half of the Golestan population are men, and about half live in urban areas.

This study was conducted using data obtained from the GPCR during the years 2004–2013. The GPCR collects information on all cancer cases from all public and private diagnostic and therapeutic centers, including hospitals, laboratory/pathology and imaging centers, and some private specialists' offices in Golestan province. In order to minimize underestimation, the GPCR also collected information from medical centers and registry centers of neighboring provinces, especially Tehran, Mazandaran, and Khorasan Razavi. Data were collected by well-trained cancer registry staff of the GPCR both actively (by regular visits to all centers to abstract data) and passively (by receiving regularly cancer-related mortality data from the death registry of the health department of Golestan University of Medical Sciences (GOUMS)). Data linkage methods were considered to match death registry data with the file of registered cancer cases to identify additional unreported cases, classified as death-certificate-only (DCO) cases. The GPCR registered only primary cancer cases and secondary tumors resulting from invasion or metastasis based on the IARC standards [27]. The third edition of the ICD code (ICD-O-III) was used to classify cancer cases in terms of anatomical site and histology of tumors [28]. As the quality indices, the proportion of cases with microscopic verification (MV%) and cases diagnosed by death certificate only (DCO%) were calculated routinely. The details of the GPCR procedure have been published recently [20].

CanReg software was used for data entering, quality control and data analysis [29]. Age-standardized incidence rates (ASRs) (per 100,000 person-years) were calculated based on the World standard population in year 2000 in 18 5-year age classes (0–4, 5–9…, 85+) [30]. Information about the population of Golestan was obtained from the statistics office of the Deputy of Health of GOUMS. The time trends of the ASR as well as the age-specific incidence rates were calculated. Average annual percentage change (AAPC) and the corresponding 95% confidence intervals (95%CIs) were calculated by Joinpoint software (version 4.6.0.0) [31]; $p < 0.05$ was considered statistically significant. The GPCR protocol was approved by the GOUMS ethics committee.

Table 1
Number, crude rate and age standardized incidence rates (ASR) (per 100,000 person-years) of breast cancer in women; Golestan province, Iran (2004–2013).

	Number	Crude rate	ASR*
Residence Area			
Total	2106	24.1	29.1
Urban	1449	34.4	39.6
Rural	657	15.5	18.4
Year			
2004	111	14.1	18.3
2005	153	19.1	25.2
2006	183	22.5	27.5
2007	224	27.1	31.8
2008	215	25.6	30.4
2009	213	25.2	29.7
2010	225	26.3	31.0
2011	234	26.7	28.9
2012	263	29.4	33.7
2013	285	31.0	31.7

* ASRs were calculated using Segi's [30] World standard population.

3. Results

A total of 2106 new breast cancer cases were diagnosed in Golestan province during 2004–2013. Most women with a breast cancer diagnosis lived in urban areas (1449 cases, 68%) in comparison with rural areas (657 cases, 31%) (Table 1). The mean (SD) age at diagnosis was estimated at 46.8 (13.0) years. The GPCR quality factors were calculated as the proportion of cases with microscopic verification (MV = 76.2) and cases diagnosed by death certificate only (DCO = 2.1%).

The overall ASR of breast cancer (29.1 per 100,000 person-years) showed a statistically significant increasing trend (AAPC: 4.4; 95%CI: 1.2–7.8; p = 0.013) (Fig. 1) and it was significantly higher in urban (39.6) than in rural (18.4) areas (p = 0.002) during the 10-year study period (2004–2013). The trends of breast cancer by residence area are shown in Table 2.

The age-specific incidence rates (per 100,000 person-years) of urban and rural populations showed that the increasing breast cancer incidence starts in younger age groups (≥20 years) (Fig. 2). The temporal trends of the age-specific incidence rates based on Joinpoint analysis illustrated significant increasing trends in breast cancer incidence among young women, including the age groups 20–29 (AAPC = 10.0; 95%CI:1.7–19.0; p = 0.02) and 30–39 years (AAPC = 5.1; 95%CI:1.4–9.0; p = 0.01) (Fig. 3, Table 2). Our results also suggested a significant increase in age-specific rates of breast cancer among older women, especially those in the age group 60–69 years (AAPC = 9.3; 95%CI:1.5–17.8; p = 0.02) (Table 2). The analysis also showed geographic variations in incidence of breast cancer in Golestan province with hotspots located in the western area (Fig. 4).

4. Discussion

Several studies indicate that breast cancer incidence rates have been rising in many countries in Asia, Africa and South America [32]. Our

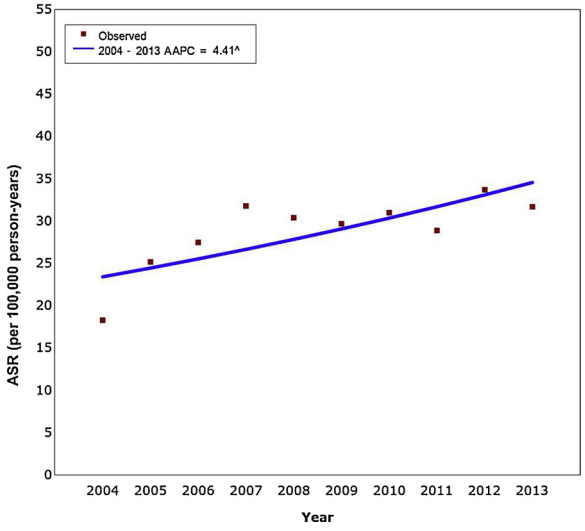

Fig. 1. Time trending of the age-standardized incidence rates (ASRs) of breast cancer in women, Golestan province, Iran (2004–2013).
^ Indicates that the average annual percentage change (AAPC) is significantly different from zero at the level alpha = 0.05.

Table 2
The Average Annual Percent Change (AAPC), Confidence Interval (CI) and p-value of breast cancer by age groups and residence area in women; Golestan province, Iran (2004–2013).

	AAPC	Confidence Interval (CI)		P-value
		Lower CI	Upper CI	
Age groups (years)				
20–29	10.0^	1.7	19.0	0.02
30–39	5.1^	1.4	9.0	0.01
40–49	5.0^	0.2	10.1	0.04
50–59	5.8	−0.3	12.2	0.06
60–69	9.3^	1.5	17.8	0.02
> =70	−4.4	−9.2	0.6	0.08
Residence area				
Urban area	3.8^	0.3	7.4	0.03
Rural area	4.3^	0.6	8.1	0.03

^ indicates that the AAPC is significantly different from zero at the alpha = 0.05 level.

study presents an overview of breast cancer incidence rates and trends among women in Golestan province during the period 2004–2013.

The incidence rate of breast cancer in our population was 29.1 per 100,000 person-years, which was comparable with those reported from other Asian populations (28.2 per 100,000 person-years) [33]. These rates are relatively low when compared with the rates reported in populations of North America and Western Europe [2]. In general, developed countries have higher breast cancer rates than low- and middle-income countries, and Asian populations have lower incidence rates than Western populations [2]. These differences in incidence rates are likely due to differences in the prevalence of risk factors, such as family history, reproductive factors and lifestyle factors, and access to and availability of early detection including screening [33–36].

We found a significant increasing trend in the incidence rates of breast cancer in our population during the 10-year study period, which is in concordance with the reported increase in breast cancer incidence rates in several other countries [33]. Changes in women's lifestyle—including delayed first birth, decreased parity, increasing levels of overweight and obesity and physical inactivity as the consequences of urbanization and westernization—may have contributed to increasing the risk of breast cancer in Golestan province and elsewhere [36]. Recent studies in Iran have concluded that the prevalence of obesity in Iran has increased, especially in women [37,38], and fertility rates have declined, likely due, at least in part, to the national family planning program of recent decades [39].

We also observed statistically significant increasing temporal trends of breast cancer among young women (20–40 years). While risk factors for breast cancer occurring in young women are not entirely understood, there are studies suggesting that birth weight, growth rate in childhood, early-age menarche, and genetic predisposition all affect risk [40–42]. Comparison between incidence rates of breast cancer between Asian and Western populations indicate higher rates among Asian women < 40 years of age than amongst Western women in the same age groups [12,14,43].The peak age for breast cancer diagnosis among Asian women is in the 4th decade of life (varying by country), which is similar to our results, whilst in Western countries the mean age at diagnosis is in the 6th decade of life [14,35]. Several studies, including a recent Asian study, indicated that women with breast cancer diagnosed at younger ages have a genetic predisposition to the disease [12,44,45]. Therefore, different approaches need to be considered in order to prevent breast cancer or detect it early in each age group, especially in young women [12]. Increasing awareness of breast cancer risk factors, signs and symptoms should be considered as a priority in breast cancer control planning, especially in our younger female population [46,47].

Our results also indicated the significant increasing trends in age-specific rates of breast cancer in the 60 s age group, which may be due to several factors such as the use of menopausal hormones, increasing levels of overweight and obesity, amongst others [48–52]. We found non-significant decreasing trends in incidence of breast cancer in women aged > 70 years. This may be due to increasing trends in incidence and mortality of cardiovascular diseases in this age group [53].

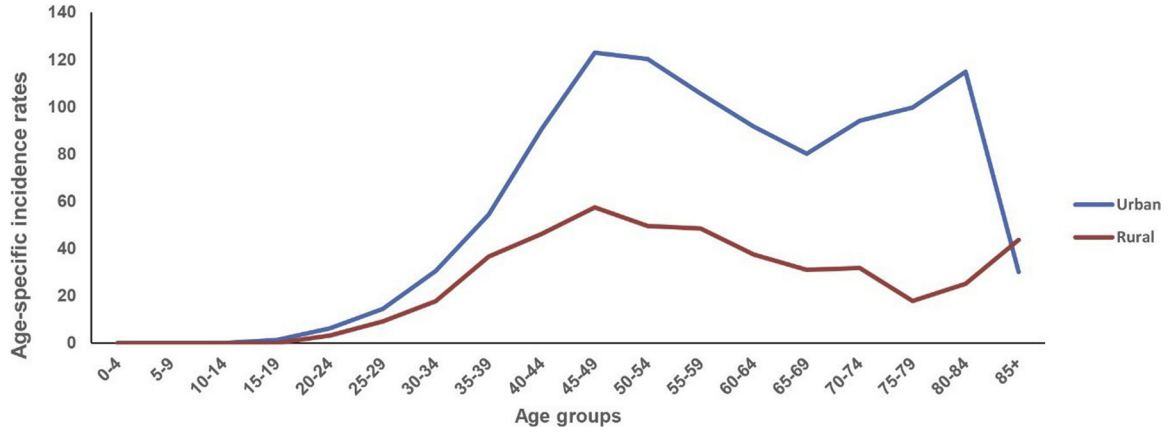

Fig. 2. The age-specific incidence rates (per 100,000 person-years) of breast cancer in women by residence area, Golestan province, Iran (2004–2013).

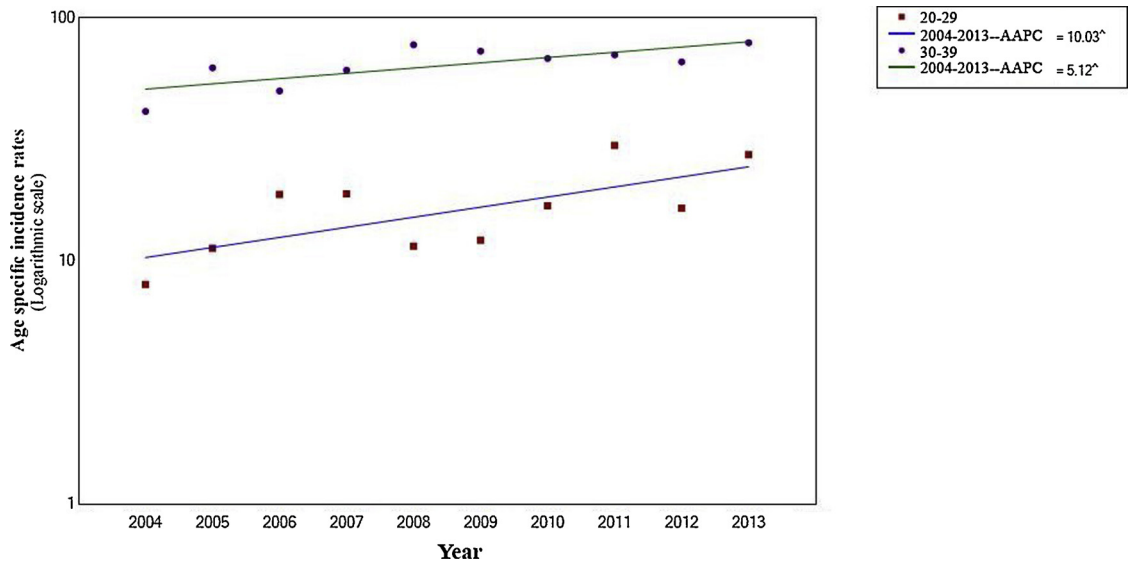

Fig. 3. Joinpoint analysis of temporal variation in age-specific rates (per 100,000 person-years) of breast cancer in young women (age groups 20–29 and 30–39 years) in Golestan province, Iran (2004–2013).
^ indicates that the average annual percentage change (AAPC) is significantly different from zero at the level alpha = 0.05.

As our study was based only on data from the cancer registry, we did not have information on risk factors other than age and place of residency (urban or rural); other studies are needed to understand specific risk factors for breast cancer in this population.

In our study, breast cancer incidence rates were significantly higher amongst women living in urban areas than amongst those in rural areas, which is in line with the findings of other studies [54,55]. Reasons for such differences may include diagnostic bias, as women in urban areas may have easier access to healthcare facilities [56,57], as well as differences in the prevalence of risk factor related to lifestyle, reproductive factors, and overweight and obesity [35,58].

Women living in western areas of Golestan province had higher incidence rates than those living in eastern Golestan. These differences may be due to urbanization, as the city of Gorgan, which is the capital of the province, is located in the western area. Other possible explanations of the differences in incidence may be related to differences in population ethnic groups. Turkman and Fars are the two major ethnics residing in the eastern and western parts of Golestan province, respectively [59]; these groups may present differences in genetic susceptibility to breast cancer, as well as differences in other risk factors [48,60,61], as demonstrated elsewhere. The information about ethnicity is not available in the GPCR database. Therefore, we could not perform analysis by ethnicity, which is a limitation of our study. Future studies should, if possible, include data on ethnicity in this region.

In conclusion, our result showed an increasing trend of breast cancer incidence in Golestan province during the years 2004–2013 in all age groups, starting in women aged ≥20. Incidence rates were higher in the western area of Golestan and in women living in urban areas. This may be due to the related life-style and genetic risk factors. In order to prevent and control breast cancer, further studies are needed to identify risk factors relevant to this region and to design breast cancer control polices in all age groups, especially in young women.

Authorship contribution

AF: Conceptualized and designed the study; edited and critically reviewed manuscript; SH-H: collaborated in analysis; wrote the manuscript; FS, FG-K: collaborated in data processing; interpreted results; critically reviewed manuscript; SR, VK, AJ: interpreted results; critically reviewed manuscript; SS, RH: collaborated in collection of data; critically reviewed manuscript; MN-T, EW: edited and critically reviewed manuscript; collaborated in quality control; GR: initiated, conceptualized and designed the study; performed statistical analysis; wrote the manuscript; All authors read and approved the final manuscript.

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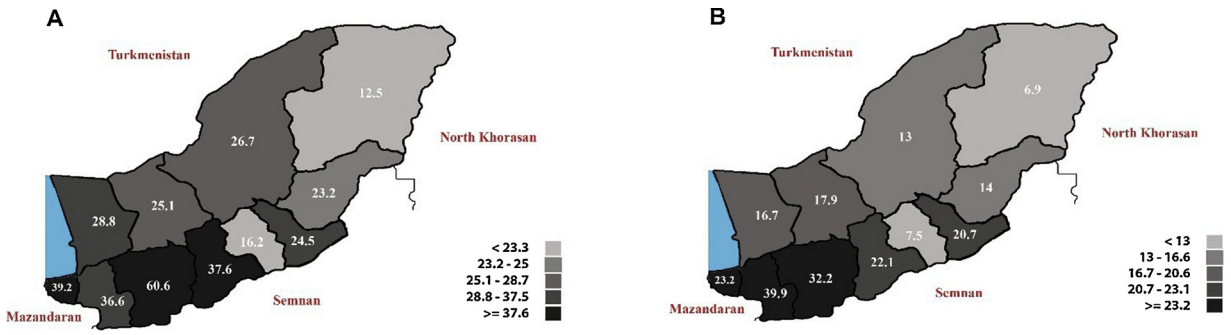

Fig. 4. Age-standardized incidence rates (ASRs) (per 100,000 person-years) of breast cancer in Golestan province, Iran (2004–2013). (A) Urban area; (B) rural area.

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