

RESEARCH ARTICLE

Epidemiological Pattern of Breast Cancer in Iranian Women: Is there an Ethnic Disparity?

Negar Sadat Taheri¹, Sepideh Bakhshandeh Nosrat², Mohsen Aarabi¹, Mohammad Naeimi Tabiei³, Elham Kashani², Siamak Rajaei⁴, Sima Besharat¹, Shahryar Semnani¹, Gholamreza Roshandel^{1*}

Abstract

Introduction: Northeastern Iran is known as a high risk area of upper gastrointestinal cancers. Recent reports have suggested a declining trend for these cancers as well as an increase in the incidence of other malignancies including breast cancer. Our present aim was to describe the epidemiological pattern of breast cancer in this region during 2004-2009. **Methods:** All new cancer cases from public and private diagnostic and therapeutic centers of Golestan province were registered. A structured questionnaire was prepared and used based on the standards of the International Association of Cancer Registries. The international classification of diseases for oncology was considered for coding. Age standardized incidence rates (ASR) of breast cancer were calculated. **Results:** A total of 11,038 new cancer cases were registered during 2004-2009, of which, 1,101 (10%) were females with breast cancer. The median age of the breast cancer patients was 46 years. The ASR for breast cancer was 28 per 100,000 person-years. We found an unusual rapid increase in breast cancer rate at the age of 25 years. The ASR of breast cancer was significantly lower in females from Turkmen ethnicity and those from rural areas (P value <0.01). **Conclusion:** Our study showed high rate of breast cancer in Golestan province of Iran. We found an unusual peak of breast cancer in young women. So, the age of starting screening programs may need to be revised in this area. The rate of breast cancer was significantly lower in women from Turkmen ethnicity. Further studies are warranted to clarify the role of important determinants, especially regarding the ethnic disparity, on breast cancer in this region.

Keywords: Breast cancer - epidemiology - ethnic disparity - Iran

Asian Pacific J Cancer Prev, 13 (9), 4517-4520

Introduction

Advances in controlling communicable diseases, made the non-communicable ones including cancers as one of the most important challenge in health systems. As other parts of the world, cancers are major public health problems in Iran. According to reports of the Iranian Ministry of Health and Medical Education (MOHME), cancer is the third cause of death in following coronary heart disease and accidents (Goya, 2007; Naghavi et al., 2009).

Breast cancer is the most common cancer in women representing 1.38 million new cases (23% of all reported cancer cases in women) in 2008 worldwide (Ferlay et al., 2010). It is the leading cause of cancer death in women (Mathers et al., 2008; Ferlay et al., 2010). The range of mortality rates (approximately 6-19 per 100,000), made it the fifth most common cause of cancer-related death overall (Mathers et al., 2008; Ferlay et al., 2010). Since 1990, mortality from breast cancer in the United States and other industrialized countries has been decreasing at

the rate of approximately 2.2% per year. In the United States, this decline has been attributed both to advances in adjuvant therapy and to increasing use of screening mammography, in approximately equal measure (Berry et al., 2005). Several variables have been identified as risk factors for breast cancer in women, including age, lack of childbearing or breastfeeding, higher hormone levels, race, economic status, family history of breast cancer, lifestyle, diet, weight, alcohol intake and smoking (Möller et al., 2003; Yavari et al., 2006). The incidence of breast cancer increases with age, doubling about every 10 years until the menopause, when the rate of increase slows dramatically (Pisani et al., 2002; Singh et al., 2003).

Despite a marked decrease in mortality rate of breast cancer, especially developed countries, it is still a major challenge for health policy making in developing countries such as Iran. In Iran, breast cancer ranks first among female cancers comprising 24.4% of all malignancies in women (Sadjadi et al., 2005). According to the report of the International Agency for Research on Cancer (IARC) (globocan-2008), the age standardized incidence and

¹Golestan Research Center of Gastroenterology and Hepatology, ²Department of Gynecology and Obstetrics, ³Department of Health, ⁴Department of Surgery, Golestan University of Medical Sciences, Gorgan, Iran *For correspondence: roshandel_md@yahoo.com

mortality rate of breast cancer in Iranian females were 18.4 and 8.9 per 100,000, respectively (Ferlay et al., 2010). In studies conducted in different parts of Iran, five-year survival rate of breast cancer ranged from 51 to 75 percent (Babaei et al., 2005; Mousavi et al., 2006; Yaghmayee et al., 2007; Fouladi et al., 2011). The result of a study from Tehran, Iran suggested that the disability adjusted life years (DALY) for breast cancer (during 1998-2001) was 4252 years (Mousavi et al., 2006).

Golestan province is located in the northeast of Iran. About 90% of Golestan population is from two ethnic groups including Fars and Turkmen. High incidence rates of upper gastrointestinal cancers were reported from this region, especially in Turkmen ethnicity (Mahboubi et al., 1973; Kamangar et al., 2007). As the first step of cancer control program, Golestan population-based cancer registry (GPCR) was established in this region. It has been approved as a voting member of the international association of cancer registries (IACR) since 2007.

Preliminary results of the GPCR showed that breast cancer is the most common malignancy in Golestan females and its increasing trend made it a major health problem in this area (Semnani et al., 2008; Roshandel et al., 2012). In this paper we will describe the specific epidemiologic pattern of breast cancer as well as some of its determinants including ethnicity in Golestan province of Iran.

Materials and Methods

Case definition: Only primary breast cancer cases were registered in the GPCR. Invasion and metastasis of primary tumors to other organs were not registered. Standards of the IARC were used to register malignant breast tumors.

Case finding: During a period of 6 years (2004-2009), information on newly diagnosed (incident) breast cancer cases were collected by GPCR team from all public and private diagnostic and therapeutic centers of the whole province, including hospitals, pathology laboratories, diagnostic radiology clinics and some of the specialist physicians' private offices. In order to minimize loss of data, we also obtained information from medical centers and regional registries in neighboring provinces including Khorasan Razavi, Mazandaran and Tehran.

Data collection: The registry staffs regularly visited centers and collected data of breast cancer cases. In some centers data was collected passively. Information about cancer related deaths was obtained from the death registry at the health department of Golestan University of medical sciences (GOUMS) and additional unreported cases, classified as death certificate only (DCO) ones, were identified with matching this data against the file of registered cancer patients. We check and compare ten percent of questionnaires with the original documents in the source centers to verify the accuracy and completeness of the abstracting process. The third edition of the international classification of diseases for oncology (ICD-O-III) was used for coding anatomical site and histology of the tumor (Fritz et al., 2000). Duplicate cases with the same information including last name, first name, age,

father's name, topography of tumor, place of residence and year of diagnosis were initially checked and eliminated before entering them into the database.

Statistical analysis: Data was entered into the Persian version of CanReg4 software, and IARC check program was used for data checking. Age standardized incidence rate (ASR) of breast cancer was calculated using the 18-groups world population (0-4, 5-9... >85) and reported per 100,000 person-years. Incidence rates were compared using the Poisson regression analysis in STATA-8 software. P values of less than 0.05 were considered statistically significant.

Golestan population data: Population data was obtained from provincial census done by health department of GOUMS in 2006.

Ethical issues and confidentiality: The ethics committee of GOUMS approved the GPCR protocol. We considered confidentiality measures to ensure the preservation of anonymity of the cancer cases, the best quality of registry data, and the best possible usage of the data.

Results

A total of 11,038 new cancer cases were identified over the period from 2004 to 2009. Of these, 1101 (10%) were females with breast cancer. The median (inter-quartile range) of patients' age was 46 (16) years (ranged between 20-88 years). Patients' characteristics have been summarized in Table 1. 69.4% of these patients lived in urban area. In 826 (75%) of the breast cancer cases, the diagnosis was based on histopathology (Table 1).

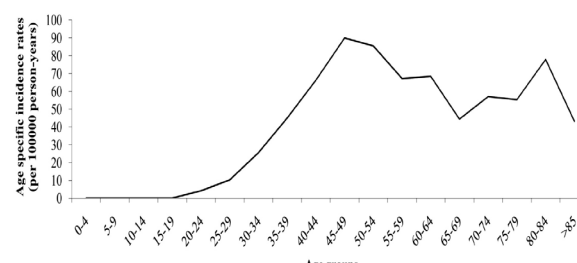


Figure 1. Age Specific Incidence Rates of Breasts Cancer in Golestan Province of Iran During 2004-2009. Table 1. Characteristics of Females with Breast Cancer in Golestan Province of Iran (2004-2009)

Variables	No.	%
Method of diagnosis:	Death certificate only	27 2.5
	Clinical	108 9.8
	Para-clinical investigation	139 12.6
	Histological examination	827 75.1
Place of residents:	Urban area	764 69.4
	Rural area	337 30.6
Ethnicity:	Turkmen	233 21.2
	Fars and Others	868 78.8
Age groups:	20-29	74 6.7
	30-39	243 22.1
	40-49	381 34.6
	50-59	234 21.3
	60-69	95 8.6
	70-79	56 5.1
	>80	18 1.6

The ASR for breast cancer was 28 per 100,000 person-years. The rate of breast cancer was significantly higher in urban (39.2) than rural area (17.5) (P value <0.01). Age specific incidence rates of breast cancer are shown in Figure 1. As figure 1 show, an unusual rapid increase was seen in age specific incidence rate of breast cancer from age 25 years. Then after a decreasing, the second peak was occurred from the age 65 years. ASR of breast cancer was significantly lower in Turkmen females (17.05) than females from Fars and other ethnic groups (31.13) (P value <0.01).

Discussion

Our study showed high rate of breast cancer (28 per 100,000 person-years) in Golestan province. Although the rate of breast cancer is lower than that of developed countries, but it seems to be relatively high when compared to developing regions of the world (Ferlay et al., 2010). According to the globocan-2008 report, the estimated incidence for breast cancer in Iran was 18.4 per 100,000 person-years (Ferlay et al., 2010). The ASRs of breast cancer in other provinces of Iran including Kerman, Gilan and Ardebil were reported as 16.9, 12.6 and 7.6 per 100,000 person-years, respectively (Sadjadi et al., 2009). So, the rate of breast cancer in Golestan province was considerably higher than those reported for Iran as well as other provinces.

We also found an increase in the ASR of breast cancer in Golestan province comparing to previous reports from this region. The incidence rate of breast cancer in Golestan province during 1996-2000 was reported as low as 15.7 per 100,000 person-years (Sadjadi et al., 2009; Semnani et al., 2006). This change in the rate of breast cancer (from 15.7-28 per 100,000 person-years) may represent a true increasing trend of this cancer during the last decade. Life style change toward westernized patterns (e.g. change in reproductive behavior, age of marriage, dietary habits, body mass index and physical activity) may be considered as possible explanation for this increasing trend. But, breast cancer is a chronic disease and such a rapid increasing (doubling during about 10 years) cannot be completely explained by the above mentioned factors. Another explanation may be the differences in methodology and techniques of data collection between the present study and the previous one. Increasing the availability of diagnostic and therapeutic services in Golestan province is another reason for unusual increasing in the rate of breast cancer. Anyway, our results showed a high rate as well as an increasing trend of breast cancer in Golestan province of Iran. It can be concluded that by decreasing the rate of upper gastrointestinal malignancies, breast cancer tends to be a major health problem in northeastern Iran. Therefore, health policy makers should be aware of this point and consider it as leading priority of health system in this region. It is necessary to implement controlling programs for this disease in our area. Determination of risk factors and conducting screening programs may be considered to achieve this goal.

We found significant lower rate of breast cancer in

women from Turkmen ethnicity. Previous studies reported contrasts in patterns of incidence of breast cancer by race. The incidence of breast cancer was higher in blacks (Hankey et al., 1994). The reasons for the lower rate of breast cancer incidence in Turkmen females have not yet been well defined. The rate of life style change is considerably lower in Turkmens than other ethnic groups in our region. So, lower rate of westernization (change in reproductive behavior, dietary habit, body mass index and physical activity) may be the possible explanation for lower rate of breast cancer in this ethnic group. In addition, as reported in the case of esophageal cancer (Akbari et al., 2007; Akbari et al., 2011), genetic factors may partially explain the difference in the rate of breast cancer between various ethnicities in Golestan province. Further case-control studies are needed to determine the reasons for low rate of breast cancer in Turkmen females.

The present study showed a significant higher rate of breast cancer in residents of urban areas. Similar findings were also reported in previous studies from other countries (Reynolds et al., 2005; Dey et al., 2010; Stamenic and Strnad, 2011). The most possible explanation for this difference is that life style change into westernized pattern usually occurs in urban areas.

Another important finding of this study was an unusual early rapid increasing (peak) in age specific incidence rate of breast cancer in young women (from 25 years of age). Similar finding was reported from other parts of Iran (Sadjadi et al., 2009). The results of some studies from Iran also suggested that breast cancer affects Iranian women at least one decade earlier than women from developed countries (Harirchi et al., 2000: 2004). It means that breast cancer occurs highly in active young women and this may result in increase in burden of the disease in our population. Further investigations are needed to clarify different aspects of this finding. For example, we may need to modify the age of starting breast cancer screening program. This will help to detect cancer cases in earlier stages and improve the efficacy of screening program. Increasing in survival, improving the quality of life as well as decreasing the burden of the disease may be considered as long term effects of this change.

In conclusion Our study showed high rate of breast cancer in Golestan province. Change in life style (toward westernized pattern), genetic and environmental factors are possible determinants for high rate of breast cancer in our area. We found an unusual early rapid increasing (peak) in age specific incidence rate of breast cancer in young women (at the age of 25 years). So, the age of starting screening program may need to be revised in Golestan province as well as other similar population. The rate of breast cancer was significant lower in women from Turkmen ethnicity. Further studies are needed to clarify the specific epidemiological pattern, especially the ethnic disparity, of breast cancer in this region.

Acknowledgements

This work was supported by Golestan University of Medical Sciences (GOUMS). Authors would like to thank Mrs Honeyehsadat Mirkarimi, Mr Abbas Moghadami,

Mr Reza Mohammadi and Mr Abbas Faramarzi for their efforts in data collection. We also appreciate valuable cooperation of the GPCR stuffs from Golestan healthcare centers.

References

- Akbari M, Malekzadeh R, Lepage P, et al (2011). Mutations in fanconi anemia genes and the risk of esophageal cancer. *Human Genetics*, **129**, 573-82.
- Akbari MR, Malekzadeh R, Nasrollahzadeh D, et al (2007). Germline BRCA2 mutations and the risk of esophageal squamous cell carcinoma. *Oncogene*, **27**, 1290-6.
- Babae Gh, Feyzi A, Keshavarz M, et al (2005). Study effect of various therapeutic and surgery methods on survival rate in breast cancer. *Daneshvar Journal*, **59**, 19-28.
- Berry DA, Cronin KA, Plevritis SK, et al (2005). Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*, **353**, 1784-92.
- Dey S, Soliman AS, Hablas A, et al (2010). Urban-rural differences in breast cancer incidence by hormone receptor status across 6 years in Egypt. *Breast Cancer Res Treat*, **120**, 149-60.
- Ferlay J, Shin HR, Bray F, et al (2010). GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide, International Agency for Research on Cancer, Lyon.
- Fouladi N, Amani F, Harghi AS, et al (2011). Five year survival of women with breast cancer in ardebil, north-west of iran. *Asian Pac J Cancer Prev*, **12**, 1799.
- Fritz A, Percy C, Jack A, et al (2000). International Classification of Diseases for Oncology, Geneva: World Health Organization.
- Goya M (2007). Iranian Annual Cancer Registration Report 2005/2006. Tehran: Center for Disease Control and Prevention, Iranian Ministry of Health and Medical Education.
- Hankey BF, Miller B, Curtis R, et al (1994). Trends in breast cancer in younger women in contrast to older women. *J Natl Cancer Inst Monogr*, **16**, 7-14.
- Harirchi I, Ebrahimi M, Zamani N, Jarvandi S, Montazeri A (2000). Breast cancer in Iran: a review of 903 case records. *Public Health*, **114**, 143-5.
- Harirchi I, Karbakhsh M, Kashefi A, et al (2004). Breast cancer in Iran: results of a multi-center study. *Asian Pac J Cancer Prev*, **5**, 24-7.
- Kamangar F, Malekzadeh R, Dawsey SM, et al (2007). Esophageal cancer in Northeastern Iran: a review. *Arch Iran Med*, **10**, 70-82.
- Mahboubi E, Kmet J, Cook PJ, et al (1973). Oesophageal cancer studies in the caspian littoral of Iran: the caspian cancer registry. *Br J Cancer*, **28**, 197-214.
- Mathers C, Fat DM, Boerma JT, et al (2008). The global burden of disease: 2004 update, World Health Organization.
- Möller T, Anderson H, Aareleid T, et al (2003). Cancer prevalence in Northern Europe: the EUROPREVAL study. *Ann Oncol*, **14**, 946-57.
- Mousavi SM, Mohagheghi MA, Mousavi-Jerrahi A, Nahvijou A, Seddighi Z (2006). Burden of breast cancer in Iran: a study of the Tehran population based cancer registry. *Asian Pac J Cancer Prev*, **7**, 571.
- Naghavi M, Abolhassani F, Pourmalek F, et al (2009). The burden of disease and injury in Iran 2003. *Popul Health Metr*, **7**, 357-62.
- Pisani P, Bray F, Parkin DM, et al (2002). Estimates of the world-wide prevalence of cancer for 25 sites in the adult population. *Int J Cancer*, **97**, 72-81.
- Reynolds P, Hurley SE, Quach AT, et al (2005). Regional variations in breast cancer incidence among California women, 1988-1997. *Cancer Causes Control*, **16**, 139-50.
- Roshandel G, Sadjadi A, Aarabi M, et al (2012). Cancer incidence in Golestan: Report of an ongoing population-based cancer registry in Iran, 2004-2008. *Arch Iran Med*, **15**, 196-200.
- Sadjadi A, Nouraie M, Ghorbani A, Alimohammadian M, Malekzadeh R (2009). Epidemiology of breast cancer in the Islamic Republic of Iran: first results from a population-based cancer registry. *East Mediterr Health J*, **15**, 1426-31.
- Sadjadi A, Nouraie M, Mohagheghi M, et al (2005). Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev*, **6**, 359.
- Semnani S, Roshandel G, Keshtkar A, et al (2008). Annual report of the Golestan Population-based Cancer Registry (GPCR), Peik Reyhan, Gorgan.
- Semnani S, Sadjadi A, Fahimi S, et al (2006). Declining incidence of esophageal cancer in the Turkmen Plain, eastern part of the Caspian Littoral of Iran: a retrospective cancer surveillance. *Cancer Detect Prev*, **30**, 14-9.
- Singh GK, Miller BA, Hankey BF, et al (2003). Area socioeconomic variations in US cancer incidence, mortality, stage, treatment, and survival, 1975-1999. NCI cancer surveillance monograph series, 4.
- Stamenić V, Strnad M (2011). Urban-rural differences in a population-based breast cancer screening program in Croatia. *Croat Med J*, **52**, 76.
- Yaghmayee S, Banihashemi Gh, Ghorbani R (2007). Study survival rate and effective cause on survival rate in women with breast cancer reffered to Semnan hospital in 1991-2002: using Cox regression. *Semnan Univ Med Sci*, **9**, 111-5.
- Yavari P, Hislop TG, Bajdik C, et al (2006). Comparison of cancer incidence in Iran and Iranian immigrants to British Columbia, Canada. *Asian Pac J Cancer Prev*, **7**, 86.