



Original Research



Geographic distribution of breast cancer incidence in Iran

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Abstract

Background: A geographic disparity for breast cancer (BC) incidence by provinces is introduced in Iran. Present study aimed to clarify the geographic disparity of BC incidence after considering the age and gender. **Methods:** In this ecological study data about BC incidence extracted from reports of national registry of cancer (NCR), and Disease Control and Prevention in 2008. BC incidence mapping was conducted in geographic information system (GIS). **Results:** The results were consistent with previous reports but extend the previous knowledge with regarding the age and gender. Highest age specific rates (ASRs) of BC occurred in the provinces located in Central and Northern of Iran. Tehran and Sistan & Balochestan had highest and lowest ASR for male BC and female BC respectively. **Conclusion:** given that BC occurs more in Central and Northern provinces that are mainly with high socioeconomic status (SES) levels, so it is suggested that disparity in BC incidence can be reduced through planning special programs such as education, screening, and preventive policy in provinces with high priorities.

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Keywords

Geographic distribution, Breast cancer, incidence, Iran

Introduction

Breast cancer (BC) is the most common cancer and leading cause of female mortality in the world (García Martínez et al., 2014), this represents about 25% of all cancers in women (Ferlay et al., 2015). Although BC mortality was decreased approximately 5% during the last decade, it is still a serious concern with 522,000 deaths in 2012 (Ferlay et al., 2015). Statistics showed that BC incidence is increasing in the low and middle-income countries (Tfayli et al., 2010). Iran is a middle-income country located in the Middle East. BC incidence in Iranian women is 24 case per 100,000, which is lower than of high income countries (Mousavi et al., 2007). However, regarding to lifestyle changes, the increase of life expectancy and socio-economic status, prediction models have found that the BC incidence for future decades will be increased (Mousavi et al., 2007).

BC is a multi-factorial disease, epidemiological studies have shown that the genetic, hormonal factors and environmental exposures are associated with incidence of BC (Pakseresht et al., 2009). It found that exposure to the different risk factors can lead to an uneven distribution of BC incidence (Laden et al., 1997). Iran have several geographic, climatic, ethnic, regional, racial, and cultural classifications that cause of exposure to different risk factors. It has been identified that BC incidence can be along with province disparity in Iran (Jafari-Koshki et al., 2014) but it proved that relevant covariates such as age and gender can affect the geography disparity in cancer measures (Henry et al., 2009).

Hence the present study attempts to discover the geographic distribution for age specific incidence rate of BC in both gender in Iran; determine whether geographic variation is in breast cancer incidence could be helpful for the future works; and provide an evidences for policymakers and planners for optimal allocation of resources.

Materials - Methods

This ecological study used re-analysis medical records aggregated to provinces from national registry of cancer (NCR), and Disease Control and Prevention report of ministry of Health and Medical Education for BC in 2008 (Ministry-of-Health-and-Medical-Services, 2008). Data collection by the Iranian Cancer Registry is active and pathology-based and covering the whole country's



pathology laboratories. Hospital-based and death certificate-based data have not been included. Cleaned data from province after deleting for repeated cases transmitted to Ministry of Health every 3 months.

Registered data classified into three part as follow:

- 1) patient's identity characteristics including age, gender, race and residence location,
- 2) patient's clinical history and
- 3) preclinical findings.

Data on primary location of tumor, date of cancer diagnosis, morphology, histology and diagnosis method is registered.

Statistical analysis

For each province, the average annual age-standardized incidence rate (ASR) per 100 000 person-years was calculated by the direct method using the World Standard Population (Boyle and Parkin, 1991). The data were presented using MS Excel 2010 and GIS ver 10.3.

Results

Figure 1 illustrates the spatial pattern for ASR of BC in Iran. Roughly an apparent geography variation in ASR of BC is occurred in Iran, so that higher ASR is belong to provinces located in central and northern parts of Iran. **Table 1** describes the province specific ASR of BC for both gender. ASR for Semnan, Zanjan and Kohkiloyeh & Boyerahamad was 0 for males. With overlooking three former province, highest and lowest total ASR were for Tehran (ASR=1.1) and Sistan & Balochestan (ASR=0.22) for males respectively. Tehran and Sistan & Balochestan have highest and lowest ASR for male BC and female BC respectively.

According to age distribution of BC in females as shown in **Figure 2**, BC roughly have a binomial distribution and highest incidence rate was for 55 to 59 age group. Basal Cell Carcinoma, NOS of the breast was the most common 'special' morphological subtype of breast cancer in both gender, for female and male were 6452 (76.59) and 136 (70.83) respectively.



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Figure 1. The geographic distribution of age specific rate (ASR) of breast cancer for females in Iran. A relatively variation in the ASR of breast cancer where surrounding province and along the edge of Iran have lower ASR and area near to center had higher ASR.



Figure 2. Incidence of breast cancer in females by age group in 2008; a relatively binomial distribution exists in age distribution of incidence of breast cancer.



Province	Males				Females			
Province	Frequency	CR	ASR	%	Frequency	CR	ASR	%
Semnan	-	-	-	-	88	30.7	41.5	23.3
Tehran	57	0.83	1.1	0.54	2624	40.4	55.8	33.4
East Azarbayejan	7	0.38	0.49	0.27	452	25.8	34.1	22.7
Zanjan	-	-	-	-	37	7.95	10.2	14.9
Kordestan	3	41	0.58	0.39	117	16.7	21.2	16.3
Yazd	3	0.59	0.86	0.46	112	23.3	31.4	19.4
Hamadan	2	0.23	0.34	0.19	153	18.5	24.6	22.9
Khozestan	12	0.55	0.7	0.45	643	31.1	41	26.7
Khorasan Razavi	15	0.51	0.65	0.43	598	21.4	28.8	21.5
Gilan	8	0.66	0.85	0.57	273	23.6	32.7	26.4
Mazandaran	10	0.67	0.98	0.56	423	30	39.8	28.4
Isfahan	12	0.51	0.77	0.45	607	27.1	37.3	27.7
Fars	11	0.5	0.69	0.46	489	23.5	32.2	24.8
Lorestan	6	0.7	0.88	0.62	125	15.1	20	17.6
Kermanshah	3	31	0.51	0.29	193	21.2	27.2	23.6
Ardebile	3	0.48	0.61	0.44	45	7.55	9.75	10.1
Ghazvin	3	0.52	0.74	0.56	115	20.9	27.8	26.7
Chaharmahal & Bakhtiari	1	0.23	0.27	0.25	60	14.4	18.7	21.7
West Azarbaijan	5	0.34	0.48	0.41	145	10.4	13.5	16.6
Markazi	2	0.29	0.48	0.35	96	14.6	19.9	24.9
Kerman	6	0.45	0.6	0.56	160	12.6	16.4	18.8
llam	1	0.36	0.49	0.47	25	9.4	12	17
Kohkiloyeh& Boyerahamad	-	-	-	-	19	6.2	7.2	10.7
Golestan	2	0.24	0.26	0.32	122	15.6	20.4	24
Qom	2	0.37	0.45	0.49	98	19.3	24.8	29
North Khorasan	1	0.24	0.46	0.33	50	12.7	15.8	20.1
South Khorasan	1	0.35	0.43	0.52	41	15.1	21	22
Bushehr	1	0.22	0.27	0.35	87	19.9	27	31.8

Table 1. The statistics of breast cancer according to gender and province



Hormozgan	2	0.29	0.35	0.66	95	14.3	18.6	31.5
Sistan & Balochestan	2	0.16	0.22	0.58	53	4.5	5.7	17
Total	192	0.53	0.72	0.45	8424	24.66	33.21	24.9

 Table 2. Morphological subtype of breast cancer in 2008

Gender	Neoplasm malignant N (%)	Lobular carcinoma N (%)	Basal Cell Carcinoma, NOS, N (%)		
Females	324 (3.85)	460 (5.46)	6452 (76.59)		
Males	8 (4.17)	8 (4.17)	136 (70.83)		

CR: Crude Rate,

%: Percent from all cancers that attributed to this cancer

Discussion

Our study indicated that ASRs of BC in Central and Northern provinces of Iran were higher than elsewhere. We found ASR have a binomial distribution, in women age 40 and over is increased, first and second peak is occurred in 55-59 and 80-84 years respectively.

In Iran ASRs of BC in various geographical regions were different, and the highest rate of ASR was observed in metropolitan provinces. BC is a multifactorial disease and there are several risk factors recognized for that, such as fertility rates (Ruddy et al., 2014), the first pregnancy in older age, infertility (Horn et al., 2013), socio economic status, educational level (Hogan et al., 2007), hormone use (Jung et al., 2013), alcohol consumption and smoking (Nelson et al., 2012) which have different patterns among various regions and states. Our results found Tehran and Sistan & Balochestan had highest and lowest incidence of BC, Tehran has a high SES and educational level, and Women of this city would rather have a Job outside the Home, besides, marriage and child bearing in Tehran occurs in older ages. On the contrary, Sistan & Balochestan has a low SES and educational level, and marriage and childbearing in this city occur in earlier ages.

The difference in incidence rates among various geographical regions was pointed out in several studies (de Grubb et al., 2013; Reynolds et al., 2005). Iran's Population consists of various ethnic groups so that this variety may affect the risk factors associated with incidence of BC.



Industrialization, social and economic status is also brought into account as risk factors of BC. With the rapid rate of industrialization of Nigeria, BC incidence rate among Nigerian has significantly increased over the past three decades (Alatise and Schrauzer, 2010). These results, being consistent with our findings, suggest that the regions with high ASR, have been undergoing social and economic transitions which lead to change in life style, rise in age of marriage, and increase rate of the first pregnancy at older age.

Others studies suggested that environmental factors (e.g. air pollution) influence BC risk (Brody and Rudel, 2003) and may be cause of disease clustering in some geographical regions. Several studies have reported that environmental pollutants may contribute to BC risk through destroying DNA, accelerating tumor growth rate, or increasing susceptibility to the BC (Rudel et al., 2007). In this study; Provinces with high ASR, mainly located in the central regions of Iran, in many aspects are different from the other provinces. Most industrial factories located in central provinces. The number of vehicles in these provinces is very high and air pollution is considered as the main problem (especially in Tehran).

Moreover, the regional differences in incidence of BC could be due to the differences in the early detection and availability of mammography in various regions (Edwards et al., 2010). Another reason could be the centralization of diagnostic and therapeutic interventions in metropolitan areas, so that the cases that belong to other regional areas may be referred to these provinces, where they are registered.

Our findings indicated that the incidence rate of BC is increased with aging and it reaches its peak between the ages of 55 to 59 years. The second peak was observed between the ages of 80 and 84 years. The steroid hormones directly affects the development and function of breast in reproductive years for women (between menarche and menopause) (Cancer, 2012). This hormone fall rapidly in post menopause and risk of breast cancer is decreased. Women become menopause mostly between the ages of 45 and 54 years. Late menopause is a known risk factor for development of BC; the risk of this factor in premenopausal women is 40 percent higher than that of postmenopausal women with the same age (Reeves et al., 2006). Some studies have suggested a decreased in the incidence of breast cancer as a result of decline in the use of hormone. These studies have also shown that the hormone users have a higher risk of being diagnosed with BC (De et al., 2010; Jemal et al., 2007). These results are consistent with our study. The second peak may happen due to the exogenous use of hormone in postmenopausal.

We found that BC in under 40 year old individuals has low incidence. Other studies have estimated an incidence of approximately 7% (Anders et al., 2009) which is consistent with our results. BC in under 40 year old individuals may be due to familial and genetic history, causing BC in younger ages. Both cumulative exposure to risk factors and BC incidence for under 40 year old people are low.



Our study was subjected to some limitations. We did not have access to data regarding cancer stage at diagnosis time in order to conduct a more detailed investigation. But this limitation have no high effect on geographical distribution at provincial level. Also we did not have data on age average of provinces. One of the most important advantages of this study is the use of routine data according to Population based on Cancer Registry with the coverage of 86.7 %.

Conclusion

This study determined the hot zones of breast cancer in Iran and can be considered as a guideline for policy maker in allocation of diagnostic and therapeutic interventions. Findings are demonstrated that the central and northern provinces need more attention. Increased access to screening for early detection is beneficial and cost-effective particularity in high incidence regions.

Abbreviations

ASR: Age specific rate BC: Breast cancer CR: Crude rate NCR: National registry of cancer SES: Socio-economic status

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Author contribution

FKS, EA and SK designed the study. KM, SMH and YM processed the data. EA, MS and YM performed the statistical analysis. FKS, SK and KM interpreted the results. FKS, KM, SK and EA wrote the first draft. FKS, SK and EA revised the final draft. All authors read and approved the final manuscript.



References

Alatise, O.I., and Schrauzer, G.N. (2010). Lead exposure: a contributing cause of the current breast cancer epidemic in Nigerian women. *Biological trace element research* 136, 127-139.

Anders, C.K., Johnson, R., Litton, J., Phillips, M., and Bleyer, A. (2009). Breast cancer before age 40 years. Paper presented at: Seminars in oncology (Elsevier).

Boyle, P., and Parkin, D. (1991). Statistical methods for registries. *Cancer registration: principles and methods* 95, 126-158.

Brody, J.G., and Rudel, R.A. (2003). Environmental pollutants and breast cancer. *Environmental health perspectives* 111, 1007.

Cancer, C.G.o.H.F.i.B. (2012). Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *The lancet oncology* 13, 1141-1151.

de Grubb, M.C.M., Kilbourne, B., Kihlberg, C., Levine, R.S., and Hood, D.B. (2013). Demographic and geographic variations in breast cancer mortality among US Hispanics. *Journal of health care for the poor and underserved* 24, 140-152.

De, P., Neutel, C.I., Olivotto, I., and Morrison, H. (2010). Breast cancer incidence and hormone replacement therapy in Canada. *Journal of the national Cancer Institute* 102, 1489-1495.

Edwards, B.K., Ward, E., Kohler, B.A., Eheman, C., Zauber, A.G., Anderson, R.N., Jemal, A., Schymura, M.J., Lansdorp–Vogelaar, I., and Seeff, L.C. (2010). Annual report to the nation on the status of cancer, 1975–2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer* 116, 544-573.

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., and Bray, F. (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer* 136, E359-E386.

García Martínez, L., Pollán Santamaría, M., López-Abente, G., Sánchez Jacob, M.M., García Palomo, A., González Martínez, R., Honrado Franco, E., and Martín Sánchez, V. (2014). Municipal Distribution and Trend of the Incidence of Breast Cancer in the Health Area of Leon, Spain (1996-2010). *Revista Española de Salud Pública* 88, 261-269.

Henry, K.A., Niu, X., and Boscoe, F.P. (2009). Geographic disparities in colorectal cancer survival. *International journal of health geographics* 8, 1.

Hogan, L., Ingemarsson, I., Thorngren-Jerneck, K., and Herbst, A. (2007). How often is a low 5-min Apgar score in term newborns due to asphyxia? *European Journal of Obstetrics & Gynecology and Reproductive Biology* 130, 169-175.

Horn, J., Åsvold, B.O., Opdahl, S., Tretli, S., and Vatten, L.J. (2013). Reproductive factors and the risk of breast cancer in old age: a Norwegian cohort study. *Breast cancer research and treatment* 139, 237-243.

Jafari-Koshki, T., Schmid, V.J., and Mahaki, B. (2014). Trends of breast cancer incidence in Iran During 2004-2008: A Bayesian space-time model. *Asian Pac J Cancer Prev* 15, 1557-1561.

Jemal, A., Ward, E., and Thun, M.J. (2007). Recent trends in breast cancer incidence rates by age and tumor characteristics among US women. *Breast Cancer Research* 9, R28.



Jung, S., Spiegelman, D., Baglietto, L., Bernstein, L., Boggs, D.A., Van Den Brandt, P.A., Buring, J.E., Cerhan, J.R., Gaudet, M.M., and Giles, G.G. (2013). Fruit and vegetable intake and risk of breast cancer by hormone receptor status. *Journal of the national Cancer Institute*, djs635.

Laden, F., Hankinson, S.E., Spiegelman, D., Neas, L.M., Colditz, G.A., Hunter, D.J., Manson, J.E., Byrne, C., Rosner, B.A., and Speizer, F.E. (1997). Geographic variation in breast cancer incidence rates in a cohort of US women. *Journal of the national Cancer Institute* 89, 1373-1378.

Ministry-of-Health-and-Medical-Services (2008). National Report of Cancer Registry (Health deputy, CDC, Cancer office).

Mousavi, S.M., Montazeri, A., Mohagheghi, M.A., Jarrahi, A.M., Harirchi, I., Najafi, M., and Ebrahimi, M. (2007). Breast cancer in Iran: an epidemiological review. *The breast journal* 13, 383-391.

Nelson, H.D., Zakher, B., Cantor, A., Fu, R., Griffin, J., O'Meara, E.S., Buist, D.S., Kerlikowske, K., van Ravesteyn, N.T., and Trentham-Dietz, A. (2012). Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. *Annals of internal medicine* 156, 635-648.

Pakseresht, S., Ingle, G., Bahadur, A., Ramteke, V., Singh, M., Garg, S., and Agarwal, P. (2009). Risk factors with breast cancer among women in Delhi. *Indian journal of cancer* 46, 132.

Reeves, G.K., Beral, V., Green, J., Gathani, T., Bull, D., and Collaborators, M.W.S. (2006). Hormonal therapy for menopause and breast-cancer risk by histological type: a cohort study and meta-analysis. *The lancet oncology* 7, 910-918.

Reynolds, P., Hurley, S.E., Quach, A.-T., Rosen, H., Von Behren, J., Hertz, A., and Smith, D. (2005). Regional variations in breast cancer incidence among California women, 1988-1997. *Cancer Causes & Control* 16, 139-150.

Ruddy, K.J., Gelber, S.I., Tamimi, R.M., Ginsburg, E.S., Schapira, L., Come, S.E., Borges, V.F., Meyer, M.E., and Partridge, A.H. (2014). Prospective study of fertility concerns and preservation strategies in young women with breast cancer. *Journal of Clinical Oncology* 32, 1151-1156.

Rudel, R.A., Attfield, K.R., Schifano, J.N., and Brody, J.G. (2007). Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. *Cancer* 109, 2635-2666.

Tfayli, A., Temraz, S., Abou Mrad, R., and Shamseddine, A. (2010). Breast cancer in lowand middle-income countries: an emerging and challenging epidemic. *Journal of oncology* 2010.