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Ali Ahmadi [1], Rashid Ramazani [2], Tahereh Rezagholi [3] and Parvin Yavari [4]

[1]Modeling in Health Research Center, Shahrekord University of Medical Sciences, Shahrekord, Islamic Republic of Iran. [2]Ministry of Health and Medical Education, Tehran, Islamic Republic of Iran. [3]Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran.
[4]
Department of Health & Community Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran (Correspondence to: P. Yavari: p.yavari-grc@sbmu.ac.ir).

Abstract

Background: Breast cancer is the leading cancer in Iranian women, but no studies have yet been conducted on the distribution and pattern of its incidence.

Aim: To perform a spatial analysis and determine the incidence pattern of breast cancer in the Islamic Republic of Iran.

Methods: This was a cross-sectional, pathology-based study of all new female patients with breast cancer registered in the Islamic Republic of Iran in 2011 (n=10 233). Initially, crude incidence rates were calculated for each province and the whole country per 100 000 person–years. Then, a direct standardization method and World Health Organization standard population were used to adjust for age effects on a geographical scale. Stata and Arc GIS software were used to calculate incidence rates and conduct spatial analysis.

Results: The mean (standard deviation) age of the patients was 50.9 (12.6) years. The national age-standardized incidence rate for breast cancer in women was 29.88 per 100 000 person–years, with a range of 5–72 in different provinces. The clustering incidence pattern was observed in Mazandaran, Tehran, Alborz, Isfahan and Markazi Provinces (P

Conclusion: These findings may help to establish etiological hypotheses of cancer causation and identify spatial anomalies in cancer incidence or registration in the Islamic Republic of Iran. Our findings may also aid further research on the possible explanations for these clusters and associations.

Keywords: Cancer, incidence rate, incidence pattern, geographical information, system, Iran

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Introduction

Breast cancer is the most common cancer in women in developed and developing countries, including the World Health Organization Eastern Mediterranean Region (1). Breast cancer is a major health problem in Asian and Arab countries including Qatar (2–4), Saudi Arabia, Iraq and Bahrain (5–7). In the Gulf Cooperation Council states (United Arab Emirates, Bahrain, Saudi Arabia, Oman, Qatar and Kuwait), breast cancer was the most common type of cancer, (24.2% of the total) in 1998–2009. The mean age-standardized rate (ASR) for breast cancer was 20.4 cases per 100 000 women, and ranged between 16.9 per 100 000 in Saudi Arabia and 55.9 per 100 000 in Bahrain (8). Cancer, after cardiovascular diseases and accidents, is the third leading cause of mortality in the Islamic Republic of Iran (9). Burden of disease is measured by disability-adjusted life years (DALYs). The more DALYs that are associated with a disease or injury, the greater the burden. This time-based measure combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health. The DALYs for breast cancer in Iranian women were 75 811 years in 2009 (10). Globocan 2012 reported the crude rate of breast cancer incidence as 26.3, ASR as 28.1 and mortality rate due to breast cancer as 9.9 per 100 000 person–years in the Islamic Republic of Iran (11).

Cancer incidence patterns vary in different populations and are associated with occupational, environmental, social, cultural, ethnic, geographic, nutritional and other unknown factors (12-14). Cancer distribution also varies in different provinces in the Islamic Republic of Iran. The incidence of cancer is higher in Ardabil (14), Mazandaran (15) and Kurdistan (16) than in other provinces. Another study found that the incidence of oesophageal, gastric, colorectal and liver cancer was clustered in Northern Islamic Republic of Iran (17). To investigate and understand cancer epidemiology, geographic information systems (GISs) and spatial analysis may be helpful. Visual display of breast cancer information using a GIS can assist in communication with policy-makers and the community. Using this tool, we can access more accurate, more tangible, and location-based descriptive and analytical data (18,19).

To the best of our knowledge, no reliable study of the incidence pattern and spatial distribution of breast cancer at a national scale has been conducted in the Islamic Republic of Iran. Breast cancer ranks first among cancers diagnosed in Iranian women but no studies have been conducted on the distribution and pattern of its incidence (20). To evaluate cancer registry and adopt a population-based strategy to prevent breast cancer on a national scale, spatial analysis should be conducted as well. This study was conducted to do a spatial analysis and determine the incidence pattern of breast cancer in Iranian women.

Methods

Study design

In this pathology-based, cross-sectional study, we enrolled all new female patients with breast cancer in the Islamic Republic of Iran in 2011 (n=10 233). The workflow of pathology-based cancer registries in the Islamic Republic of Iran is as follows. First, pathologically definite diagnosis-based data of breast cancer registries are collected from different sources (clinics, histology and cytology centres and laboratories across each province, hospitals, death certificates, and forensic medicine offices). Then, the data are entered into the cancer registries databases in the health centre of the province and duplicate cases are deleted. The registry report is sent to the Office of National Cancer Registry of Ministry of Health and Medical Education, Tehran. At the national scale, patients are classified by province of residence, national identification number, and year of cancer incidence, and the data are corrected if necessary. Again, duplicate cases are deleted. In this way, each patient is registered only once and added to the data of the province where they live. The data are sent at specified intervals to provincial health centers. That explains why pathology-based national reporting of cancer registry in the Islamic Republic of Iran is not up to-date and it takes at least 2–3 years to identify duplicate cases, and to separate and finalize the updated data by province.

The quality of pathology-based cancer registry in the Islamic Republic of Iran is satisfactory

according to formal and public reports, and it is mandatory by the law approved by the Iranian Islamic Consultative Assembly. Hence, all pathologically definite cases of cancer are registered and reported. The Iranian Ministry of Health and Medical Education offers any necessary training at various levels of the health system, and cancer cases are registered, coded and reported. Therefore, the available data for breast cancer is the best choice to determine the current status of the disease in absence of a national, population-based cancer registry system covering the whole country. The approach to cancer registry in the Islamic Republic of Iran is such that reliable and accurate data can be gathered from the whole country. According to the available reports, the coverage proportion of the pathology-based cancer registry increased from 18% in 1998 to 60% in 2004 and then to 83% in 2008.

We used the data from 884 of 896 (98.5%) pathological centers in the Islamic Republic of Iran that sent their reports (20). Definitive diagnosis was made by pathological examination of tissue samples. In this cross-sectional study, the codes ICD10 (C50.0–C50.9) were used for diagnosis of breast cancer (21).

Statistical analysis

Initially, crude incidence rates per 100 000 individuals were calculated for each province and the whole country. To calculate incidence rate, we used data on the female population released by the National Census of the Statistical Center of Iran in 2011 (22) (Table 1). Age was considered a confounder in the analysis. Then, a direct standardization method and WHO standard population were used to adjust for age effects on a geographical scale (23). For spatial analysis, global and local indicators of spatial autocorrelation (LISA), Moran's I, and Getis–Ord test were used (19,24–26). For mapping the breast cancer rates in the Iranian provinces, 7 options (manual, equal interval, defined interval, quantile, natural breaks, geometrical interval and standard deviation) in the "classification" menu (ArcGIS Software) were used for categorization and justification. In accordance with the software guidelines, skewed data and a similar study (27), we adopted "quantile" and used 4 classifications to map incidence rates. For mapping spatial analysis and identifying the clusters, we selected "conceptualization of spatial relationships" from the "spatial statistic tools" menu and the maps were automatically reported in 7 categories. Stata version 12 software (Stata Corp. College Station, TX, USA) and Arc GIS Desktop: version 9.3.1 (Iran National Cartographic Center) were used to analyse the data and P

Results

In pathology cancer registry, 10 233 new female patients with breast cancer were registered in the Islamic Republic of Iran in 2011. The mean (standard deviation; SD) age of the patients was 50.9 (12.6) years. The age range at breast cancer development was 15–106 years. The ASR of breast cancer was 5–72 per 100 000 person–years in different provinces. The ASR of breast

cancer in the Islamic Republic of Iran as a whole was 29.83 per 100 000 population. Figure 1 illustrates the ASR of breast cancer in the provinces.

The null hypothesis of “Incidence pattern of breast cancer is random in Iran” was tested and not confirmed. The incidence pattern of breast cancer in was obtained by clustering (Moran’s index = 0.579, P Figure 2).

The highest standardized incidence rate (72 per 100 000 population) was derived in Alborz and Tehran Provinces (Table 2). The clustering incidence pattern of breast cancer was observed in Mazandaran, Tehran, Alborz, Isfahan and Markazi Provinces (P Figure 3).

Discussion

We reported for the first time in the Islamic Republic of Iran a clustering pattern of breast cancer incidence. The provinces at a higher risk of breast cancer incidence or with no suitable registry of breast cancer were identified and reported, which will be of interest to future epidemiological studies. In the Islamic Republic of Iran, national registry of cancer cases is not population-based and is implemented by a variety of approaches such as cohort studies and is pathology based. In some northern provinces, particularly Golestan, cancer cases are registered by a population-based approach and cohort studies. Cancer cases are registered by population-based approach in a few regions of Fars Province and in the capital Tehran. In other regions, cancer registry is pathology based according to healthcare system (27,28).

The methodology adopted to identify clustering patterns of breast cancer in the present study is similar to that in a study in Saudi Arabia reporting clusters of other cancers. In Saudi Arabia, female breast cancer had statistically significant, positive global Moran’s I index values, indicating potential clustering. The Anselin’s local Moran’s I analyses showed small significant clusters of lung cancer, prostate cancer and Hodgkin’s disease among men in the eastern region and significant clusters of thyroid cancer in women in the eastern and Riyadh regions (5). In Bahrain, the ASR decreased from 58.2 per 100 000 in 2000 to 44.4 per 100 000 in 2010 (7), which is higher than the total incidence rate of breast cancer in the Islamic Republic of Iran (29.83 per 100 000 population), but lower than the rate in Tehran and Alborz Provinces (72 per 100 000 population). The incidence of cancer (8.8 per 100 000 population) in Kurdistan Province was lower than that obtained in the present study (15.8 per 100 000 in Kurdistan and 29.8 per 100 000 in the Islamic Republic of Iran) (16). A study in Northern Islamic Republic of Iran reported that the spatial incidence pattern of oesophageal, gastric, colorectal and liver cancers was clustering in Golestan and Mazandaran Provinces (17), but no clustering was seen

for breast cancer. The present study, however, indicated that in Mazandaran Province, breast cancer incidence pattern was also clustering, which is not consistent with the previous study. This inconsistency can be explained by our comparison of all provinces in the Islamic Republic of Iran in the present study, while only 2 provinces (Babol Cancer Registry data) were investigated in the study of Northern Islamic Republic of Iran (17).

A study in Shiraz, Islamic Republic of Iran reported that the incidence rate of breast cancer in women was 13 per 100 000 population (26), which is lower than the incidence rate (29 per 100 000 population) in the present study. In Fars province, 4569 cancer patients were studied from 2001 to 2009, indicating gastric cancer (26) and colorectal cancer (27) as the most prevalent cancers in men and women. In these studies, the incidence pattern of gastric and colorectal cancers was reported to be clustering. In one of these studies in Fars Province the incidence pattern of breast cancer was derived as random (27). Although it is not consistent with the overall incidence pattern of breast cancer derived in our study, it agrees with the breast cancer incidence pattern in Fars province, which was obtained as random. This finding confirms a study of Fars province and implicitly indicates the acceptable reliability of the present study's data (27).

Advances in spatial technology have enabled epidemiologists to develop detailed maps and adopt spatial cluster statistics to gather data on patterns of disease. Spatial cluster analysis of disease has traditionally been used to find potential causes. However, spatial epidemiologists, thinking of latency and mobility, are increasingly focusing on spatial factors of healthcare availability and demographics affecting disease diagnosis (25-27). The incidence rate of breast cancer in Tehran in the present study (72 per 100 000 population) is higher than previously found (17.261 per 100 000 population) (28). Our study findings are consistent with a study in Ilam, Western Islamic Republic of Iran (29).

ASR in the present study was higher than that reported by the Globocan 2012 estimate (29.8 vs 28.1 per 100 000 population) (11). This difference can be explained by the fact that, in our study, the numerator represented all cases of breast cancer in 2011, the denominator represented the population of women according to the Iranian national census, and the WHO standard population was used to conduct standardization. However, in Globocan 2012, the data from different cancer registries, such as Ardabil in 2007, East Azarbaijan in 2006 and Tehran in 2001, as well as Golestan in 2008 were used to estimate ASR as the weighted average of the local rates for the Islamic Republic of Iran (11). It is recommended that Globocan in their following reports and Iranian researchers in studies conducted in the future pay attention to this difference and its potential causes. It seems that because ASR in the current study was calculated for all provinces in the Islamic Republic of Iran, it is closer to the real ASR of breast cancer in Iranian women. However, this requires more detailed investigation and potential explanation in future studies.

The clustering pattern of breast cancer in Tehran, Alborz, Mazandaran, Markazi, Isfahan, Gilan and Semnan Provinces can be explained variously. First, carcinogenic environmental factors and risk factors for breast cancer are possibly higher in these provinces. Second, breast cancer may have a higher rate or might be registered more completely in these compared with other provinces. Overall, the higher incidence of breast cancer in some provinces should be further examined to find potential explanations. In the conducted analysis, the spatial scale was the province. Urban and rural areas are consistently distributed across the country except for Tehran and Alborz where urban areas are more frequently distributed. Faster or more precise diagnosis may be one of the most important potential factors for the differences in the incidence rates among different provinces, and women in more urbanized provinces (Tehran and Alborz) are likely to have more convenient access to medical services, which may influence registration of breast cancer. However, it is not clear whether the clustering incidence of breast cancer in the present study was attributable to the approach to cancer registration, diagnosis and treatment centres, education, income and economic status in the Islamic Republic of Iran. In accordance with previous studies, certain factors contribute greatly to patients' referral and early diagnosis of cancer, including easy access to insurance, migration, age, gender and ethnicity (28,29). It is likely that in the provinces without satisfactory medical services and long distances to travel, the population may have inadequate knowledge about the risks and the need for early medical attention. No or irregular provision of diagnostic services should be considered one of the possible contributors to the differences in the incidence rates observed in different provinces. The reported clustering should therefore be viewed with caution and consideration of the above factors. If this clustering is real, it is necessary to find the causes and focus on the provinces with clustering incidence of breast cancer and if the clustering is due to under-registration in some provinces, it is necessary to address further and improve the population-based registry of breast cancer in the Islamic Republic of Iran.

The findings of this study could help with adoption of an appropriate strategy for programmes of cancer registry and prevention in the Islamic Republic of Iran. The trend in breast cancer incidence can be investigated by gaining access to these data. This should be considered in future studies. The strength of the present study was the use of GIS to provide decision makers with precise, tangible and location-based descriptive and analytical data. In this study, the clustering incidence pattern of breast cancer supports a greater emphasis on explaining the clustering in the Islamic Republic of Iran; whether the clustering is real or due to under-registration in some provinces. However, the pattern of breast cancer incidence derived in the present study does not correspond to the nationwide regular and uniform pattern. Spatial data can be represented as discrete points or polygonal. Therefore, the approach to analysis may be different. For discrete point data, exact latitude and longitude coordinates of patients' living place, and for polygonal data, the coordinates of latitude and latitude in terms of geographical region of living place (province) are required. As the exact latitude and longitude coordinates of the patients' living place were unavailable, we failed to draw the map of interest, which can be plotted only in population-based and/or cohort studies where the exact addresses are available. Some strengths of cluster analysis are: discovering and identifying incidence

pattern of breast cancer in Iranian women (random, distributed or clustering); identifying the accumulation spots of breast cancer; and finding clues to the determinants of causes of accumulated breast cancer cases in certain areas. Following this analysis, researchers can seek to establish whether the clustering is due to an actual increase in the number of cases of breast cancer or under/over-registration in different regions. The results of cluster analysis assist in developing and offering other hypotheses to investigate breast cancer-associated factors.

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Profil d’incidence et analyse spatiale du cancer du sein chez les femmes iraniennes : utilisation des applications du Système d’information géographique

Résumé

Contexte : Le cancer du sein est le cancer le plus répandu chez les femmes iraniennes, mais aucune étude n’a été réalisée à ce jour sur la distribution et le profil de son incidence.

Objectif : Procéder à une analyse spatiale et déterminer le profil d’incidence du cancer du sein en République islamique d’Iran.

Méthodes : Il s’agissait d’une étude transversale portant sur les caractéristiques pathologiques de toutes les nouvelles patientes atteintes d’un cancer du sein enregistrées en République

islamique d'Iran en 2011 (n=10 233). Dans un premier temps, les taux bruts d'incidence ont été calculés pour chaque province et dans l'ensemble du pays pour 100 000 personnes-années. Ensuite, une méthode de standardisation directe et la population type définie par l'Organisation mondiale de la Santé ont été utilisées pour ajuster les effets de l'âge sur une échelle géographique. Les logiciels Stata et Arc GIS ont été mis en œuvre pour calculer les taux d'incidence et conduire une analyse spatiale.

Résultats : L'âge moyen des patientes était de 50,9 ans (ET 12,6). Le taux d'incidence standardisé sur l'âge était de 29,88 pour 100 000 personnes-années à l'échelle nationale, et était compris entre 5 et 72 dans différentes provinces. Une agrégation de l'incidence a été observée dans les provinces de Mazandéran, de Téhéran, de l'Alborz, d'Ispahan et de Markazi (p

Conclusion : Ces résultats pourraient permettre de poser des hypothèses étiologiques sur les causes de cancer du sein et d'identifier les anomalies spatiales en matière d'incidence ou enregistrement du cancer en République islamique d'Iran. Ils pourraient également aider la recherche future à déterminer les possibles explications de ces agrégations et associations.

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