Spatio-temporal Mapping of Breast and Prostate Cancer in South Iran During 2014-2017

Mahdieh Montazeri
Kerman University of Medical Sciences

Benyamin Hoseini
Mashhad University of Medical Sciences

Neda Firouraghi
Mashhad University of Medical Sciences

Fatemeh Kiani
Mashhad University of Medical Sciences

Hosein Raouf-Mobini
Mashhad University of Medical Sciences

Adele Biabangard
Mashhad University of Medical Sciences

Ali Dadashi
Zanjan University of Medical Sciences

Vahideh Zolfaghari
Mashhad University of Medical Sciences

Leila Ahmadian
Mashhad University of Medical Sciences

Saeid Eslami
Mashhad University of Medical Sciences

Robert Bergquist
World Health Organization

Nasser Bagheri
Australian National University

Behzad Kiani (✉ Kiani.Behzad@gmail.com)
Mashhad University of Medical Sciences  https://orcid.org/0000-0002-8816-328X

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Abstract

Background:

Breast and prostate cancers are the most common gender-specific malignancies. In developing countries, screening of all population at risk of cancers is impractical because of the healthcare resource limitations. Thus, determining the high-risk areas of Cancers might be an important step to conduct a screening program at high-risk areas. This study explores potential high-risk clusters in the incidence pattern of breast and prostate cancers in southern Iran.

Methods:

This cross-sectional study was conducted in the province of Kerman, South Iran. Patient data were aggregated at the county and district levels and the incidence rate per 100,000 people for both breast and prostate cancer were calculated. We used the natural break classification with five classes to produce descriptive maps. A spatial clustering analysis (Anselin Local Moran's I) was used to identify potential clusters and outliers in the pattern of these cancers from 2014 to 2017.

Results:

The Age-Standardised Incidence Rate of breast cancer showed an increase from 29.93 to 32.27 cases per 100,000 people and prostate cancer from 13.93 to 15.47 cases per 100,000 during 2014–2017. Cluster analysis at the county level identified high-high clusters of breast cancer in the North-West of the province for all years, but the analysis at the district level showed high-high clusters for only two of the years. Furthermore, cluster analysis at the county and district levels of prostate cancer also identified high-high clusters in the North-West of the province for two years.

Conclusions:

North-West Kerman had a significantly higher incidence rate of both breast and prostate cancer. These findings may help to design tailored screening and surveillance systems. Furthermore, this study generates new hypotheses to test potential relationships between environmental risk factors and incidence of cancers in areas with higher cancer risk.

Background:

The majority of deaths occur due to non-communicable diseases such as cancers, the second leading cause of death worldwide (1). The world's ageing population leads to a significant increase in the incidence of chronic diseases such as cancers (2). Furthermore, human exposure to multiple risk factors has increased the burden of cancers worldwide (3). Despite advances in timely diagnosis and medical
treatment of cancers in recent years, malignancies in middle to low-income countries are expected to almost double by 2030 compared to high-income nations (4). If cancer is diagnosed promptly, life can be prolonged and the cancers sometimes cured, leading to considerably lower burdens of these diseases (5, 6). However, health systems, particularly in developing countries, cannot screen all people to identify cancer patients in the early stages of the disease. It seems that one of the most efficient ways of decreasing the cost of screening, finding the people at risk and implementing more efficient diagnostic strategies is identifying high-risk geographical areas (7). Investigating high-risk areas should also provide valuable knowledge to scientists about the aetiology of some cancers (3).

Breast and prostate cancers are the two most common gender-specific malignancies across the world (8). Furthermore, these cancers cause the highest disability-adjusted life years (DALYs) (9). Risk factors for breast and prostate cancers are diverse and interrelated. These include genetic (10), social-economic (11) as well as lifestyle and environmental factors (12). Further, there is, for example, an interaction between environmental risk factors and other risk factors for cancers (13, 14). There is a spatial variation in environmental risk factors and this variation may lead to heterogeneity in the pattern of cancers in a given geographic catchment area. Studies by Wang et al. (2017) and Wang et al. (2020) found a significant spatial variation of prostate cancer incidence and prostate cancer-specific mortality in Pennsylvania, USA. They evaluated potential effects of individual and county-level risk factors and found that spatial variations in prostate cancer-specific mortality rates existed in Pennsylvania with a particularly high risk in the Pen State catchment area (15, 16). County-level health and environmental factors might contribute to spatial heterogeneity in prostate cancer-specific mortality in the study area. A study by Olfatifar et al. (17) examined spatial clustering of breast cancer at the provincial level in Iran between 2004 and 2010. Their results highlighted that breast cancer incidence varied across the provinces (17). At the same time, Rohani-Rasaf et al. (18) detected some high-risk regions in the capital of Iran Tehran for both breast and prostate cancers. Most studies in Iran applied spatial analyses at very coarse level (province scale) and this is, to best of our knowledge, the first study that investigates the spatial clustering in the pattern of breast and prostate cancers incidence at a finer geography scale in the South part of Iran.

Geographical information system (GIS) is a useful tool for identifying high-risk areas of cancer occurrence, also investigating the environmental effects on cancer incidence (19–21). GIS compounds spatial and non-spatial data together producing a geodatabase, making it possible to perform spatial analyses using this data structure. For example, spatial autocorrelation is a method of exploratory spatial data analysis which allows detecting spatial dependence or autocorrelation in spatial data (22). There are two kinds of spatial autocorrelation methods; global methods and local statistics. Global methods are more sensitive to departures from the null hypothesis, which examine whether data, here patients, are randomly distributed or follow a spatial pattern. They identify spatial structures in the pattern of cancer incidence but do not determine where the clusters are. Local cluster statistics, on the other hand, quantify spatial autocorrelation and clustering, but only in limited areas. These methods may find high-high risk (HH) regions, high-low (LH) regions, low-low (LL) regions and low-high (LH) regions of incidence within a study area. HH and LL regions are defined as the target area surrounded by areas with similar incidence
rates while for HL and LH regions, the target area is surrounded by areas with dissimilar cancer incidence rates. In other words, the HH and LL indicate clusters, while the HL and LH indicate outliers (23). This study aims to identify the spatial pattern of breast and prostate cancers and to investigate the potential clustering in gender-specific incidents pattern of these cancers in south Iran between 2011–2017.

**Method**

*Study Area:*

This study was conducted in the province of Kerman, located in south Iran (Fig. 1). The first administrative level of Iran subdivisions is the province, each of which is further subdivided into counties that are subdivided into districts. Our study area contains 22 counties and 58 districts. Kerman covers an area of 183,285 km² and has, according to the National Census of 2015, a population of 3,164,718 people (24).

*Data Sources:*

Data were obtained from two different sources with three different spatial scales (individual, county and district). The individual patient data were obtained through the population-based cancer registry of Kerman. They were geocoded and aggregated to both county and district. The digital maps (county and district) were obtained through the mapping organisation of the country.

We used a crude incidence per 100,000 people and the age-standardised rate (ASR) per 100,000 people for the descriptive statistics.

*Spatial Analyses:*

For the thematic maps, we used the natural break classification with five classes. The natural breaks classification method is a data clustering method designed to determine the best arrangement of values into different classes. This is done by seeking to minimise each class’s average deviation from the class mean, while maximising each class’s deviation from the means of the other groups. In other words, the method seeks to reduce the variance within classes and maximise the variance between classes (25). For spatial visualisation, the crude incidence per 100,000 people and the ASR per 100,000 people were used.

*Spatial Cluster Analysis:*

Incidence rates of breast and prostate cancers were calculated using total population and number of cancer cases in each county and district of the province. There were 22 counties and 58 districts in the study area. The Local Moran's I statistic (26) was performed to quantify spatial autocorrelation of cancers frequency at county and district level. This test calculates a z-score and p-value to determine whether the apparent similarity (a spatial clustering of either high or low values) or dissimilarity (a spatial outlier) is more pronounced than one would expect in a random distribution. The null hypothesis states that the cancers are randomly distributed across the study area.
We used ArcGIS, v. 10.5 (ESRI, Redlands, CA, USA) for spatial analyses and Microsoft Excel 2016 for the descriptive analyses.

Results:

There were 1350 breast cancer patients, 42 cases were male, and 478 prostate cancer patients during the period March 2014-March 2017 in the study area. Table 1 shows crude incidence per 100,000 people and ASR per 100,000 people of breast and prostate cancer in the province of Kerman, Iran during the period March 2014-March 2017. Both breast and prostate cancer ASR increased by 29.93 to 32.27 and 13.93 to 15.47 from 2014 to 2017, respectively.

Table 1

|                      | March 2014-March 2015 | March 2015-March 2016 | March 2016-March 2017 |
|----------------------|-----------------------|-----------------------|-----------------------|
|                      | Number | Crude rate | ASR  | Number | Crude rate | ASR  | Number | Crude rate | ASR  |
| Breast               | 438    | 26.64      | 29.93| 445    | 28.71      | 32.49| 467    | 29.73      | 32.27|
| Prostate             | 151    | 9.82       | 13.93| 128    | 8.42       | 11.29| 199    | 12.36      | 15.47|

Figure 2 reveals the age distribution of breast cancer patients in the study area. As shown in the figure, the number of women (after 25 years of age) who get breast cancer increased rapidly. Furthermore, the incidence of most breast cancers occurred in the 50–54 years age group in the 2014–2015 period, in the 65–69 age group in the 2015–2016 period and in the 75–79 age group between 2016 and 2017.

Figure 3 reveals the age distribution of prostate cancer patients in the study area. After 45 years of age, the number of men with diagnosed prostate cancer increased a way similar to that of breast cancer for women after 25 years of age. In contrast, however, the ascent of this cancer in relation to seniority was considerable in all years from 2014 to 2017.

Figure 4 shows the space-time pattern of breast cancer incidence at the county level. The descriptive maps revealed that the incidence was highest in the North-East of the province from March 2014 to March 2017. However, as the cluster maps show, there were HH clusters of breast cancer in the North-West of the province from March 2014 to March 2017; furthermore, there was LL cluster in the South-East of the province from March 2014 to March 2015 and March 2016 to March 2017.

Figure 5 shows the space-time pattern of breast cancer incidence at the district level. The descriptive maps revealed that the incidence was highest in the North stretching towards the centre of the province. However, as cluster maps show, there were HH clusters of breast cancer in the North-West of the province from March 2014 to March 2015 and March 2016 to March 2017; furthermore, there were LL clusters in the North-East of the province from March 2014 to March 2015 and March 2016 to March 2017.
Figure 6 shows the space-time pattern of prostate cancer incidence at the county level. The descriptive maps revealed that the incidence was highest in the North-East. However, as the cluster maps show, there were HH clusters of prostate cancer in the North-West of the province from March 2014 to March 2016; furthermore, there were LL clusters of prostate cancer in the South-East and East of the province from March 2014 to March 2017.

Figure 7 shows the space-time pattern of prostate cancer incidence at the district level. The descriptive maps revealed that the incidence was highest in the North-East of the province from March 2015 to March 2016. However, there was a HH cluster of prostate cancer in the North-West of the province from March 2014 to March 2015 and some HH clusters in the North-West tending to the centre from March 2016 to March 2017.

**Discussion:**

The main aim of this study was to explore the spatio-temporal patterns of breast and prostate cancer incidence and to the best of our knowledge, this is the first study in the province of Kerman to assess spatial variations in the pattern of breast and prostate cancers. The study revealed a high incidence rate of both breast and prostate cancers in the Northwest of the province while it was low in the Southeast part of the Kerman province. The number of people with breast and prostate cancer increased considerably after 25 and 45 years of age, respectively. Further investigations are needed to assess the drivers in the high-risk areas identified in northwest Kerman. They might be associated with environmental factors and lifestyles (12), poor access to cancer-specific services (27), hereditary reasons (10), and/or socio-economic inequalities (28, 29).

Environmental risk factors such as air pollution (30–32) and heavy metals (33, 34) could be linked to the geographic outcome disparities in breast and prostate cancer incidence. We found high-risk areas of breast and prostate cancer in the Northwest of the province during 2014–2017. Kerman is located in the Southeast of the Iranian volcano-plutonic copper belt (35) and arsenic contamination is one of the most significant environmental concerns in the Northwest of this province (36). The Sarcheshmeh copper industrial plant, the biggest copper mine of Iran, is located in the Kerman’s Northwest and this area could be contaminated by heavy metals such as arsenic. Field studies report widely distributed travertine rocks in the North of the Sarcheshmeh copper mine and indicated that highly concentrated range of arsenic exists in the travertine rocks (36). This arsenic could move into the water system and contaminate the drinking water in nearby urban and rural communities (36, 37). In these areas, the arsenic concentration is higher than the World Health Organisation (WHO) drinking water recommended values (36, 38, 39). Indeed, arsenic-enriched water is one of the critical challenges in Kerman (36). Arsenic has been categorised as a Group 1 carcinogen factor by the International Agency for Research on Cancer (IARC) (40) and some studies associate arsenic and breast cancer (41–44); its presence in the study area is thus a potential explanation for the increased incidence of breast cancer found. However, other studies did not show any significant association with arsenic (45, 46). The power of this association can change due to local and individual diversities (43).

Furthermore, several studies indicate also a significant association...
between arsenic-enriched water and prostate cancer incidence (44, 47, 48). Thus, high incidence of both breast and prostate cancers in the North-west of Kerman may be associated with arsenic contamination and this should be investigated in future studies.

Increased levels of copper may play a significant role in the initiation of prostate cancer (33). Copper smelting and toxic discharges have led to soil pollution, especially in the region of the smelting plant in Sarcheshmeh Copper Complex. Studies indicated that most contaminated areas are located in the wind directions (49), Which is particularly disturbing is that the polluted areas are also used as grazing land so the toxic elements of soil enter the food chain. These elements include various heavy metals in addition to copper and arsenic, such as lead, molybdenum and cadmium (49). Therefore, soil, water and nutrition of Rafsanjan and the adjacent townships, located the North-West of the province, are subject to the potential negative effects of these heavy metals. Indeed, previous studies have found associations between heavy metals and breast and prostate cancers (50–52). The current study strongly recommends to examine the hypothesis which exposure to heavy metals, especially arsenic and copper, may associate with high incidence of gender-specific cancers in the northwest of Kerman Province.

Air pollution measures, such as particulate matter, have been shown to be associated with risk of breast cancer (31, 32). Further studies to confirm the effects of airborne pollution, especially particulate matter, on the risk of breast cancer is suggested. Fazzo et al. (2016) used a spatial approach to estimate the industrial air pollution impact on 17 selected neoplasms in Priolo, Sicily Italy. The territory around the industrial Sicilian area of Priolo, Italy, was defined as a contaminated site of national priority for remediation because of diffuse environmental contamination caused by large industrial settlements. The study found a higher incidence of breast cancer in the contaminated area compared to the rest of the province (53).

Previous studies highlighted that poor access to health care services lead to poor health outcomes (54, 55) such as increased incidence of cancer (27, 56). The high incidence of gender-specific cancers in some regions of the study area may be due to their considerable distance from the provincial capital with limited cancer screening programmes. On the other hand, parts of the study area in the South had the lowest incidence of both breast and prostate cancers, although they were located even further away from the provincial capital. However, proximity to health care services does not directly translate into access because of potential factors such as poor socio-economic status and low level of education that could be associated with poor access (54). GIS enable researchers to assess the revealed access to cancer services through combing spatial and non-spatial factors (55, 57, 58) and the results suggest measuring access to cancer prevention programmes in the study area as the first step of examining this hypothesis. Previous studies have highlighted the impact of the socio-economic status on the differences in breast and prostate cancers incidence (59–61). Assessing the impact of socio-economic status on the geographic disparities of the gender-specific cancers incidence in the study area can be done by analysing the overall spatial structure or identifying high-risk areas. This also warrants further studies.
Hereditary cancer syndromes, a type of inherited disorder in which there is a higher-than-normal risk of certain types of cancer, are caused by mutations in certain genes passed from parents to children (62–66). Indeed, certain patterns of cancer may be seen within families, e.g., hereditary breast (65) and lynch syndrome (63). Hereditary cancer screening programmes (67–69) have made it possible to detect many of the approximately 5–10% of breast cancers caused by a genetic predisposition (70, 71) and ultimately to prevent them before they occur. Also, there are studies that assessed risk of prostate cancer associated with hereditary cancer syndromes. This highlights the risk of prostate cancer in people with a family history of cancer that strongly associates with early-onset disease (66). We strongly recommend researchers and policymakers to perform hereditary cancer screening and genetic testing in high-risk areas of the province and assess the association of the results with the high incidence rate of both breast and prostate cancers in these areas.

Spatio-temporal cluster analysis plays a significant role in visualising and quantifying geographical variation in patterns of disease incidence. This study used Local Moran's $I$ to identify the high and low clusters as well as spatial outliers of breast and prostate cancer. Global Moran's $I$ and Getis-Ord General $G$ statistic are the Global clustering methods which investigate the level of spatial autocorrelation in disease patterns. While Local Moran's $I$ and Getis-Ord $G_i*$ are the local cluster analyses which can indicate the locations of the clusters. Although Getis-Ord $G_i*$ statistic is used for identifying hot and cold spots, Local Moran's $I$ method is also effective for assessing statistically significant spatial outliers (72). Thus, it was applied over other local methods (26, 73) and successfully assessed disease hotspots (74, 75). If a study wants to use these methods to analyse the spatial pattern of incident data, it should consider aggregating the incident data into polygons. The main question here is the geographical scale that should be used for aggregation because it could affect the results. In this study, we conducted the analyses in both in county and district level.

**Conclusions:**

We identified a great deal of spatial variations with significant clusters in the patterns of breast and prostate cancers. This suggests that policymakers need to develop tailored prevention strategies to areas where the risk of these conditions are greater. Further, there is a need to conduct further research to test the causality relationship between environmental risk factors and cancer incidence.

**Abbreviations**

GIS
Geographical information system; HH:High-High; LL:Low-Low; HL:High-Low; LH:Low-High; WHO:World Health Organization; IARC:International Agency for Research on Cancer;

**Declarations**

Ethics approval and consent to participate:
This study has been approved by Ethical Committee of Kerman University of Medical Sciences (number=IR.KMU.REC.1397.290).

Consent for publication:

Not applicable:

Availability of data and materials:

The cancers data have been uploaded as supplementary files. However, due to protect the patients’ data, the latitude/longitude of patients’ location has been removed.

Competing interests:

The authors declare that they have no competing interests.

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Authors’ contributions:

M.M and L.A provided the data and funding. N.F conducted spatial analyses and manuscript writing. H.R-M and A.B and F.K geocoded the data. A.D contributed to manuscript writing. V.Z performed the descriptive analyses. R.B and N.B contributed to manuscript writing and revising the text. B.H and B.K drafted the manuscript, designed the study and reviewed the literature. B.K was the research leader. The author(s) read and approved the final manuscript.

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Authors’ information:

B.K is an assistant professor at Mashhad University of Medical Sciences. He has been working on health geographical information systems and different aspects of geo-spatial data sciences.

NB is a Senior Research Fellow and spatial epidemiologist at the Australian National University (ANU) with a particular interest in geo-spatial analysis and modelling.

R.B is the editor-in-chief of the Geospatial Health Journal and has much experience in spatial epidemiology.

B.H is a faculty member at Neyshabur University of Medical Sciences and junior researcher at Mashhad University of Medical Sciences. He has been working on the health informatics projects and also has
much experience in the health outcome registries.

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Figures

Map of counties, districts and distribution of cancer (prostate and breast) patients in Kerman during 2014-2017

Figure 1

Map of counties, districts and distribution of cancer (prostate and breast) patients in Kerman during 2014-2017
Figure 2

Age distribution of breast cancer patients in the province of Kerman, Iran

Figure 3

Age distribution of prostate cancer patients in the province of Kerman, Iran
Figure 4

Breast cancer incidence map at the county level in the province of Kerman, Iran
Figure 5

Breast cancer incidence map at the district level in the province of Kerman, Iran
Figure 6

Prostate cancer incidence map at the county level in the province of Kerman, Iran
Figure 7

Prostate cancer incidence map at the district level in the province of Kerman, Iran

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ProstateData.xlsx
- BreastData.xlsx