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Original Article

Bayesian Spatial Analysis of the Incidence Rate of Patients with Breast Cancer in Southern Iran

Abbas Rezaianzadeh[1], MD, MPH, PhD; Mahnaz Hosseini-Bensenjan[2], MD; Sepideh Sephidbakht[3], MD; Sezaneh Haghpanah[2], MD, MPH; Zahra Khosravizadegan[4], MD; Naeimehossadat Asmarian[5], PhD; Mani Ramzi[2], MD

[1]Colorectal Research Center, Shiraz University of Medical Sciences, Shiraz, Iran;
[2]Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran;
[3]Medical Imaging Research Center, Department of Radiology, Shiraz University of Medical Sciences, Shiraz, Iran;
[4]Shiraz Population Based Cancer Registry, Shiraz University of Medical Sciences, Shiraz, Iran;
[5]Anesthesiology and Critical Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Correspondence:
Naeimehossadat Asmarian, PhD; Anesthesiology and Critical Care Research Center, Mohammad Rasul Allah Research Tower, Khalili Ave., Molasadra St., Postal code: 71936-35899, Shiraz, Iran
Tel: +98 71 36122263
Email: ns.asmarian@gmail.com
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Abstract

Background: In the female population, breast cancer is the most common cancer and a leading cause of cancer death. This study was designed to investigate the geographical pattern of breast cancer risk in different counties of Fars province in the south of Iran from 2001 to 2018.

Methods: In this historical cohort study, data of Shiraz Population-Based Cancer Registry between 2001 and 2018 was used. The geographical variations of breast cancer incidence rate in 36 counties of Fars province were analyzed using the Bayesian spatiotemporal model.

Results: Overall, the averages of relative risk (RR), temporal trend (TT), and δi for breast cancer were 1.59, 1.025, and 0.00 in the total female population; 1.21, 1.002, and 0.00 in the young female population (under 40 years of age); and 1.54, 1.02, and 0.00 in the female population with invasive ductal carcinoma (IDC), respectively. The steady increase in RR of breast cancer and IDC during 2001-2018 was observed in most counties located in the non-central part of the Fars geographic map. Moreover, a steady increase of young breast cancer RR was observed mainly in southern regions and some northern cities of Fars province.

Conclusion: Between 2001 and 2018 in Fars province, a steady annual increase of approximately 2% was observed in the total female population for all types of breast cancer, including IDC. High-risk areas, TTs, and changing patterns of breast cancer incidence were determined in this region. Furthermore, areas with a high risk of young breast cancer were identified, which requires special attention.

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Keywords ● Bayesian method ● Spatial analysis ● Breast neoplasms ● Incidence rate

What's Known

- In the female population, breast cancer is the most common cancer and a leading cause of cancer death worldwide.
- A spatial analysis of national cancer registry data in 2009 in Iran showed that the central provinces, including Fars, have the highest rates of breast cancer (incidence rate: 36.2 per 100,000 people).

What's New

- A steady annual increase of 2% was observed in the total female population for all types of breast cancer in Fars province during 2001-2018.
- High-risk areas, temporal trends, and changing patterns of breast cancer incidence as well as areas with a high risk of young breast cancer were determined in this region.

Introduction

In the female population, breast cancer is the most common cancer and a leading cause of cancer death both in developed and developing countries.[1] Especially in recent years, the pattern of cancer incidence has changed more towards developing countries.[2] In Iran, the Center for Disease Control and Prevention of the Ministry of Health, Treatment and Medical Education has announced that breast cancer is the most common type of cancer among Iranian women, accounting for 21% of all malignancies.[3]

During the last decades, besides increased life expectancy and aging of the population,[4] changes in the prevalence of breast

cancer-associated risk factors have contributed to the increase in the breast cancer incidence rate globally.[1] Similar to other cancers,[5, 6] the overall incidence rate of breast cancer is different all over the world and even within a nation.[7] This geographical variation can be interpreted by the difference in genetic and especially environmental risk factors. Moreover, these variations are more significant regarding age groups, topographical location of the tumor, and morphological subtypes.[8]

The average age of breast cancer occurrence in Asian women is lower than in Western countries.[7] The median age at diagnosis of breast cancer in Iranian women is 40-50 years, which is a decade earlier than over 50 years old in developed countries.[9] Most of the breast malignancies are adenocarcinoma, accounting for more than 95% of cases.[10] Invasive breast cancers are a heterogeneous group of tumors, and among them, invasive ductal carcinoma (IDC) is the most common type.[11]

Fars province located in South-West Iran is one of the most important regions regarding breast cancer (age-standardized rate of 19.12 per 100,000 persons per year for breast cancer based on a hospital-based study in 2001-2006).[8] Additionally, in 2009, the spatial analysis of national cancer registry data in Iran showed that the central provinces, including Fars, have the highest rates of breast cancer in Iran (incidence rate: 36.2 per 100,000 people).[12]

Spatial analysis helps to investigate and understand cancer epidemiology better in terms of the pattern and distribution of the disease, which leads to better communication with health policymakers.[13] Thus, this study was designed to investigate the geographical pattern of breast cancer risk using a popular full Bayesian model called BYM spatiotemporal model (overall and in young women) in different counties of Fars province in the south of Iran during 2001-2018.

Materials and Methods

Fars province consists of 36 counties located in the southwest region of Iran. According to the 2016 census reported by the Statistical Center of Iran (SCI), 4.80 million people (51% males) live in this area.[14] Figure 1 represents the geographical location of Fars province in Iran and counties of Fars province. The population at risk in each year was attained from the SCI. The population at risk (i.e. scaled 1/1000) in 2006 for the 36 counties is shown in figure 2. As indicated in this figure, Shiraz is the city with the most at-risk population overall and for individuals younger than 40 years old.

In this historical cohort study, data from the Shiraz Population-Based Cancer Registry (SPBCR) during 2001 to 2018 was used. Shiraz is the capital city of Fars province and the most known referral center for cancer care in southern Iran because the quality and accessibility of cancer diagnosis and treatment services are much better than in other counties in southern Iran. Thus, it has the largest data on breast cancer patients. The SPBCR collects data on new cancer reports from almost all of the diagnostic and therapeutic centers as well as death registries in Fars province. SPBCR is the most qualified cancer registry in southern Iran in terms of the completeness of case diagnosis, comparability, data quality, and timeliness.[15] According to the latest census, the population covered by this registry is more than five million people with a female:male ratio of 1:1.03. The majority of residents live in urban/suburban

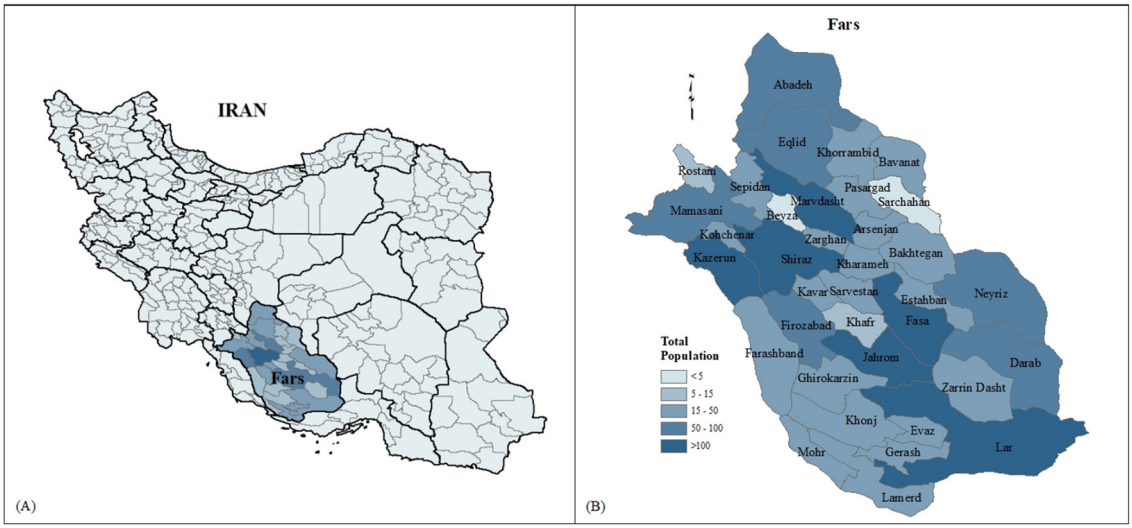

Figure 1: The geographical location of Fars province in Iran (A) and counties located in Fars province (B) (scaled 1/1000) (created using ArcGIS Desktop: Release 10.1, https://www.esri.com/en-us/arcgis/about-arcgis/overview)

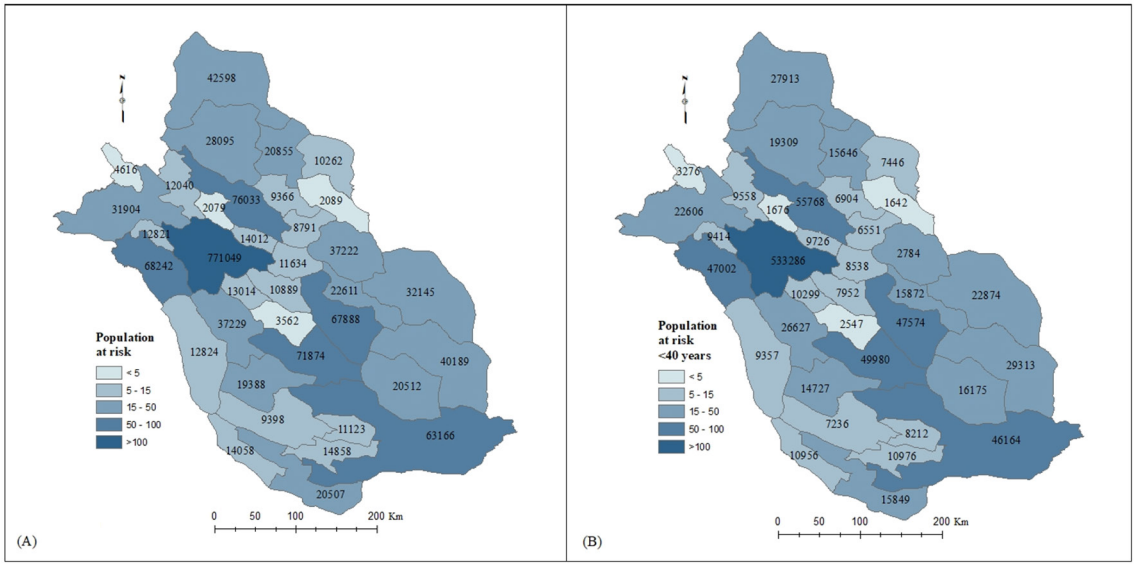

Figure 2: The at-risk population in different counties of Fars province (scale: 1/1,000); A: Total females; B: Women<40 years.

areas. Patient data including age, sex, date of birth, and date of current cancer diagnosis were collected, abstracted, and computerized by well-experienced cancer registrars. In addition, topographic and morphological data of the malignancies were abstracted and registered to be used in the third edition of the International Classification of Diseases for Oncology (ICD-O-3). Duplicated cases were identified and removed using software-based techniques.[16] An adapted version of CanReg5 software is used by SPBCR.

The study protocol was approved by the Ethical Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1401.393).

Statistical Analysis

In this study, the geographical variations of breast cancer incidence rates in 36 counties were analyzed. The observed number of new breast cancer cases in a geographic unit (county) was assumed to follow a Poisson distribution. The Bayesian spatiotemporal models by extending the BYM (Besag-York-Mollies) model are the most popular full Bayesian models that were explained in many references in detail.[17, 18] The spatiotemporal trend model can be written as:

$$\eta_{it}=\alpha+v_i+u_i+(\delta_i+\beta)t$$

In this model, as suggested by Bernardinelli and others,[19] the intercept (α) was assumed to follow an improper uniform and normal distribution with zero mean and a small variance as prior, respectively. The structured spatial (u_i) effects, the unstructured effects (v_i), and interaction between space and time (δ_i) are random effects; and the precision parameters, controlling the amount of variability for the random effects, were assumed to follow a gamma distribution (0.50, 0.0005). Outcomes calculated as relative risk $RR=exp\ (v_i+u_i)$ and temporal trend $TT=exp(\delta_i+\beta)$.

The spatiotemporal model was coded in the Open BUGS version 3.2.3[20] for estimating the parameters, and ArcGIS 10.1[21] was used to display the results on maps. We ran two chains with 1000 samples as burn-in and 10,000 samples as iteration. Convergence for the chains was confirmed by auto-correlations, trace, and densities plots.[22]

Results

Several maps of geographical variations of breast cancer incidence across the 36 counties of Fars province were generated with the BYM model, spatiotemporal trend model, and posterior estimate value of δi. In the interpretation of the maps, δi displays the difference between the global trend of incidence rate and the area-specific trend of incidence rate. δi<0 shows that this trend is less steep than the mean trend, while δi>0 shows that the area-specific trend of incidence rate is steeper than the mean trend. The exponential to the value of the time coefficient in this model, which is defined as the temporal trend (TT), was classified as >1: increasing trend and TT<1: decreasing trend over time. Moreover, different shades are proportional to the relative risk (RR) value, as darker areas show a higher RR.

The average of RR, TT, and δi for breast cancer was 1.59, 1.025, and 0.00 in the total female population, 1.21, 1.002, and 0.00 in the female population under 40 years of age, and 1.54, 1.02, and 0.00 in the female population with IDC, respectively.

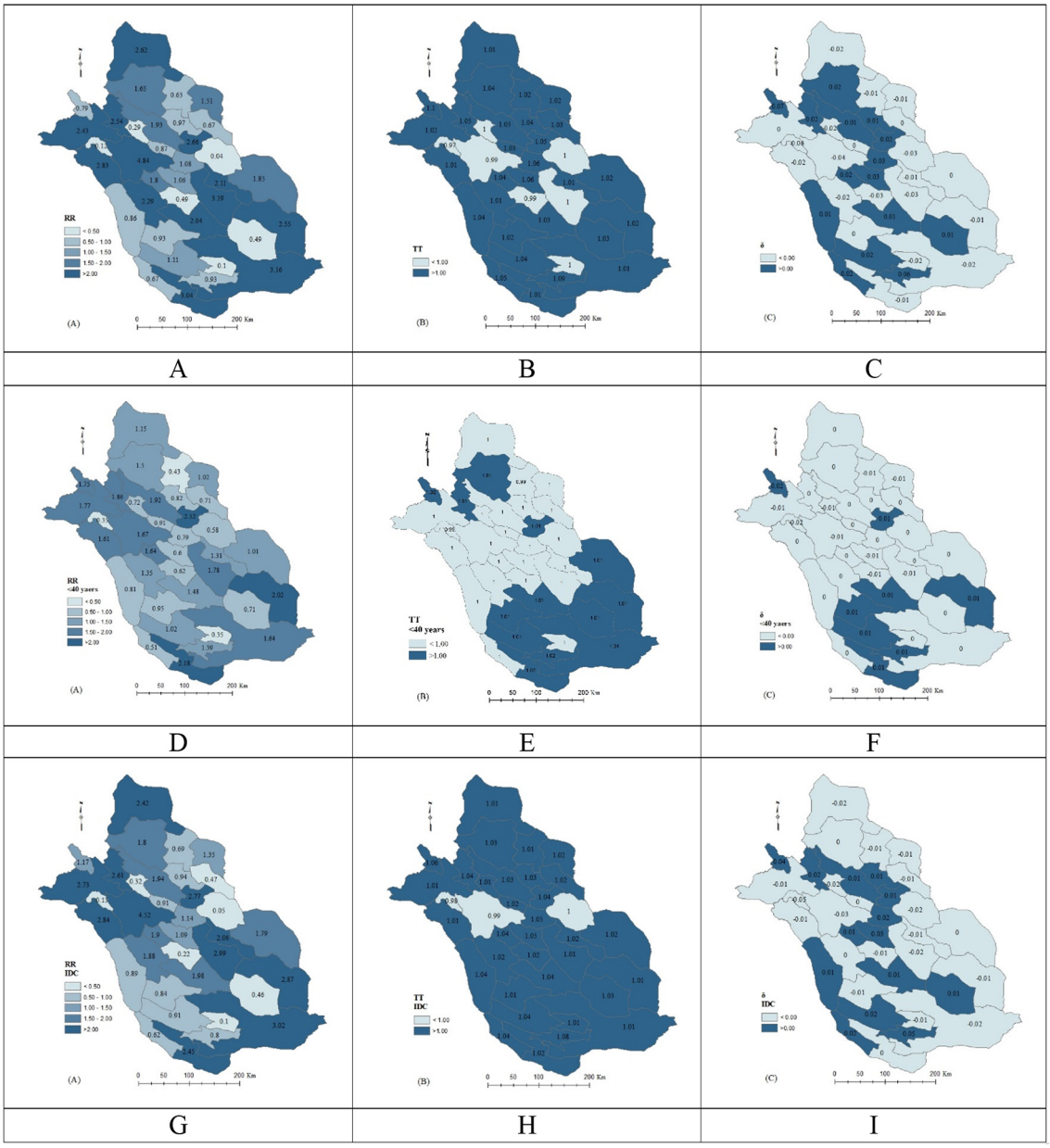

Figure 3: Breast cancer incidence rate in total female population (A-C), female population under 40 years (D-F), and IDC (G-I) across the 36 counties of Fars province with posterior mean of the spatial main effect. (A) Relative risk (RR) by the BYM model, RR>1 shows the probability of an increased relative risk. (B) Posterior temporal trend (TT) of MS incidence rate, TT>1 shows an increasing trend, and TT<1 shows a decreasing trend over time. (C) Posterior mean of the differential time effect δi. δi<0 shows that this trend is less steep than the mean trend, while δi>0 shows that the area-specific trend of incidence rate is steeper than the mean trend. (Created using ArcGIS Desktop: Release 10.1, https://www.esri.com/en-us/arcgis/about-arcgis/overview)

Figure 3A demonstrates the distribution of RR of all types of breast cancer in the female population of all age groups. The highest risk was observed in Shiraz (4.84), Fasa (3.19), Larestan (3.16), and Lamerd (3.04). Figure 3B shows the TT of breast cancer incidence rate across different counties from 2001 to 2018. The steady increase in the RR of breast cancer is observed nearly in all counties, except some counties in the central part of the Fars geographic map including Shiraz. Figure 3C represents the change of temporal patterns of breast cancer incidence rate across different counties in Fars province. Compared to the global trend, darker areas indicate that the trend in those counties is steeper, and lighter areas indicate that the trend is less steep.

For the population of women under 40 years old, Arsanjan, Lamerd, and Darab showed the highest RR: 2.52, 2.18, and 2.02, respectively (figure 3D). Moreover, TT in this subgroup was >1 in most counties in the south of Fars, and Eqlid, Sepidan, Rostam, and Arsanjan in the north of Fars, indicating a geographical shift mostly towards southern regions (figure 3E).

As shown in figure 3 (G-I), for IDC, the highest RR was detected in Shiraz (4.52), Larestan (3.02), and Fasa (2.99). Additionally, TT was >1 in all counties except Shiraz, Kohchenar, and Bakhtegan. Overall, the geographical distribution of RR of IDC, as well as its TT over time and change in temporal pattern are similar to what was observed in all types of breast cancers.

Discussion

In this study, the spatial distribution of the RR of breast cancer as well as the TT and its change over time were determined in women of all age groups and young women living in the south of Iran between the years 2001 and 2018. A steady-state annual increase of about 2% in the total female population for all types of breast cancer and IDC was observed in Fars province during 2001-2018. In young women, this increasing trend was observed at a lower rate (0.2% annually), but it is still at a constant rate.

The highest RR of breast cancer incidence in all age groups was observed in Shiraz, Fasa, Larestan, and Lamerd. The highest rate of breast cancer was previously reported in the age group of 40 to 49 years in Fars province.[8] Thus, more attention should be paid particularly to women over 40 years old with special attention to high-risk counties by increasing their awareness and improving preventive and medical healthcare facilities.

On the other hand, young breast cancer, a health concern, defined as the presence of breast cancer in younger women usually under the age of 40, should also be considered because, despite the low proportion of this cancer age group (below 5%), it usually manifests itself in more advanced stages and more aggressive types.[23, 24] A 10-year study (2004-2013) from a population-based cancer registry in northern Iran showed an increasing trend in the incidence of breast cancer among all age groups, especially among women aged 20-39 years.[25] In a study of the population of breast cancer in Fars province, it was reported that one-fifth of the population of breast cancer patients were under 30 years old.[26] In the present study, the highest RR of young breast cancer was observed in Arsanjan, Lamerd, and Darab. Moreover, this pattern was steady over time and steeper than the mean trend, which requires special attention.

IDC has been reported as the most common type of breast carcinoma in Iran[27] and Fars province,[26] and its prognosis is highly related to the receptor subtypes of breast cancer.[28] In our study, the considerable point about IDC was an increasing trend in the majority of counties across the province, which warrants further attention for the prevention and control of this aggressive type of breast cancer in Fars province.

Based on the results of this study, Shiraz showed the highest RR of overall breast cancer as well as IDC in women of all age groups possibly due to more cancer screening and cancer detection in this city. On the other hand, a change in temporal pattern over time was observed in this city for RR of all types of breast cancer as well as IDC, which can be probably the result of more attention to implementing preventive programs and health care services in Shiraz as a referral center for breast cancer and the capital of Fars province. These results underscore the importance of equity in healthcare service delivery, especially in deprived counties. A comprehensive investigation of socioeconomic inequalities in female breast cancer incidence and mortality in Iran was done by a Bayesian spatial analysis of registry data of breast cancer at a sub-national level. It revealed an increase in mean age-standardized cancer incidence versus a decrease in the mortality rate from 2000 to 2010 across provinces. After considering wealth index quintiles, higher incidence and mortality rates were observed in provinces in the wealthiest quintile. However, these provinces showed a greater decline in mortality over time than those in the poorest quintile. The authors have stated that lower incidence in poorer provinces indicates underdiagnosis or late diagnosis. Additionally, the greater decline in the mortality rates over time in provinces with higher index quintiles, despite higher mortality rates in these regions, suggests the possibility of future reversal. This highlights the importance of focusing more on prevention, access to health care, and screening programs in deprived areas.[29]

Taken together, a higher risk of breast cancer was observed in some counties, possibly due to increased life expectancy, higher rate of screening, urbanization and economic development, and more exposure to related risk factors[1, 29] including obesity,[30] physical inactivity,[31] western diet,[32] alcohol, smoking,[33] and reproductive factors such as early menopause, higher age at first marriage, short breastfeeding duration,[34] and oral contraceptive use.[34, 35] It is necessary to pay more attention to establishing the hypothesis of etiology in high-risk areas and, as a result, changing the risk factors that can be modified in these areas. Moreover, spots with increasing trends of breast cancer incidence over time were detected in some other regions. These findings are valuable

for health policymakers to prioritize the regions for resource allocation, consider preventive and educational programs, and improve medical and healthcare services in these regions. It is also necessary to improve the coverage of the cancer registry system.

The strength of this study was detecting high-risk spots of breast cancer incidence in women based on the population-based-cancer registry data and determining changes in its trend over time. Furthermore, this study had certain limitations; first, the pathology of breast cancer was not specified in more detail. Second, the immunohistochemistry of breast cancer and receptor subtypes were not recorded.

Conclusion

This study revealed the pattern and distribution of breast cancer incidence across different counties in Fars province. Between 2001 and 2018, a steady annual increase of approximately 2% was observed in the total female population for all types of breast cancer, including IDC. High-risk areas, temporal trends, and changing patterns of breast cancer incidence over 2001-2018 were determined. Moreover, areas with a high risk of young breast cancer were identified. The findings of this study can be of great interest to policymakers to implement effective strategies for breast cancer prevention and control in different areas based on the priorities set. Further epidemiological studies in high-risk areas are recommended to find the etiology and associated risk factors.

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Authors' Contribution

A.R: Study design and reviewing the manuscript; M.HB: Data gathering and drafting; S.S: Data interpretation and reviewing the manuscript; S.H: Data interpretation and reviewing the manuscript; Z.Kh: Data gathering, and reviewing the manuscript, N.A: Study concept, data analysis, and reviewing the manuscript. All authors read and approved the final manuscript and are responsible for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Naeimehossadat Asmarian, as the Editorial Board Member, was not involved in any stage of handling this manuscript. A team of independent experts was formed by the Editorial Board to review the article without her knowledge.

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