Original Article

Spatial Cluster Analysis of Stomach Neoplasms in the Center of Iran Based on a Population-Based Study, 2009-2014: Application of the Poisson-Based Probability Model

Abstract

Background: A better understanding of the spatial pattern of stomach cancer can be helpful in the implementation of preventive strategies. This study is one of the first studies to establish a study unit based on the smallest possible size for cluster analysis. This study includes a novel evaluation of spatial differences in different geographical areas of Arak. The present study seeks to discover the spatial clusters of stomach cancer from 2009 to 2014 in Arak. **Methods:** All of the addresses of the stomach cancer cases were geocoded. After that, the number of stomach cancer cases in each census block was calculated to be entered in the SaTScan software. A discrete Poisson-based probability model was used to analyze this cluster. **Results:** In Arak, there are 5502 census blocks with a population of about 526,182. The number of identified and registered stomach cancer cases with an acceptable residence address was 392. Totally, 11 stomach cancer clusters were established in the area of Arak, from these; two clusters were detected statistically significant. Relative risks of the first and second clusters were 1.75 (P = 0.01) and 17.60 (P = 0.04) and those are located within the radius of 1.73 and 0.085 km, respectively. **Conclusions:** Our results have confirmed that two areas are at a higher risk than others. However, based on the results of this study, community-based interventions in certain geographical areas can be designed to reduce and control the incidence of stomach cancer.

Keywords: *Iran, spatial analysis, stomach neoplasms*

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Introduction

Stomach cancer is the fourth most common cancer and the second cause of cancer deaths around the world.[1,2] In addition to *Helicobacter pylori*, which is one of the main risk factors for stomach cancer, other factors include smoking, obesity, high consumption of red meat, low consumption of fruits and vegetables,[3,4] and high salt intake increase the risk of stomach cancer.[3] Probably differences in the incidence of stomach cancer in different parts of the world are due to differences in the prevalence of exposure to Helicobacter and lifestyle factors in these areas.[3]

Among the people of Arak in Markazi province, there are some evidence for the possible formation of spatial clusters. Recently, cohort studies on the impacts of airborne pollutants in Europe[5,6] have shown that airborne contaminants are related to a high risk of stomach cancer in men. On the other hand, the inhabitants of Arak, which is an industrial metropolis, are closely exposed to most of industrial pollution sources. Therefore, Arak can be considered as a high-risk area in this regard, so there is the possibility of forming clusters of this disease in the city. Annual age-standardized incidence rate of SN was 13 per 100,000 population in Markazi province, Iran.[7]

Earlier studies on the design and identification of cluster disease in Iran[8-13] rely more on a provincial level unit that can hide the discovery of many of the high-risk clusters by the probability of committing ecological errors. This study is one of the first studies to establish a study unit based on the smallest possible size for cluster analysis. This study includes a novel evaluation of spatial differences in different geographical areas of Arak.

A better understanding of the spatial pattern of stomach cancer can be helpful in the implementation of preventive strategies, including the eradication of Helicobacter

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and the early detection of stomach cancer in the target population and geographical areas. The disease mapping of incidence is an important field in public health and epidemiology, which may suggest solutions to the urgent needs of health policy makers.[14]

Therefore, the present study seeks to discover the spatial clusters of stomach cancer from 2009 to 2014 in Arak, and it is being done using calculating the incidence of stomach cancer in the level of each census block, the smallest units of the census at the Population and Housing Census Organization of Iran.[15]

Methods

The population under study is the inhabitants of the metropolis of Arak with an approximately 650,000 population. Arak is an industrial metropolis with large industries such as petrochemicals, aluminum, major machineries, and so on. The city, known as the city of industrial pollutants, is located in the center of Iran. All cases of stomach cancer diagnosed from 2009 to 2014 in pathology laboratories and clinics in Arak or other cities in Iran, reported to the Cancer Registry of the Universities of Medical Sciences, have been included in the study.

The data had duplicate records in the first stage. For data cleaning and identifying the duplicates, all stomach cancer data with code C16 were independently evaluated by the two authors of this study. The data were cleaned by selecting all those cases of stomach cancer who wrote Arak as their place of residence. Then, to find the same records, they were first sorted by surname, then by name, and finally by the name of the father. Only one of the same records remained in the original data.

Eventually, 210 cases (equivalent to 35% of all the recorded cases) out of all of the cases in the population-based stomach cancer data were excluded from the final analysis, because there were not valid addresses to establish their spatial patterns.

Statistical analysis

Descriptive analysis was conduct with STATA 12.0. All of the addresses of the stomach cancer cases were geocoded based on latitude and longitude coordinates. The population in the census blocks, which are the smallest units of the census, was obtained from Statistical Center of Iran, as recorded in the 2011 census. After that, the number of stomach cancer cases in each census block was calculated to be entered in the SaTScan software (SaTScan v9.6 March 2018).[16] Scan statistics are used to find cluster disease in a spatial context. For this purpose, scanning is done gradually with a window across space. The scanning window is a circle of space. The windows with maximum likelihood can be the most likely clusters, and a *P* value for each of these clusters was calculated.

Given the nature of the data, a discrete Poisson-based probability model was used to analyze this cluster.[16] In this model, the number of patients in each location is Poisson distributed. Detected stomach cancer clusters are finally displayed using Google earth. A significant level is also determined after 9999 simulations of the Monte Carlo. A *P* value less than 0.05 was statistically significant.

For purely spatial analyses, SaTScan also identifies secondary clusters in the data set in addition to the most likely cluster and orders them according to their likelihood ratio test statistic. There will almost always be a secondary cluster that is almost identical with the most likely cluster and that have almost as high likelihood value, since expanding or reducing the cluster size only marginally will not change the likelihood very much. Most clusters of this type provide little additional information, but their existence means that while it is possible to pinpoint the general location of a cluster, its exact boundaries must remain uncertain. There may also be secondary clusters that do not overlap spatially with the most likely cluster. These are always reported. The *P* values for such clusters should be interpreted in terms of the ability of the secondary cluster to reject the null hypothesis on its own strength, whether or not the more likely clusters are true clusters or not. Hence, these *P* values are not adjusted for the fact that there may be other clusters in the data.[16]

Results

Descriptive results

In Arak, there are 5502 census blocks with a population of about 526,182. The number of identified and registered stomach cancer cases with an acceptable residence address was 392. Of these, 76% (N = 298) are men and 24% (N = 94) are women. The age of the patients in this study ranged from 25 to 111 (Mean, SD: 66, 13)

Cluster analysis

Totally, 11 stomach cancer clusters were established in the area of Arak (1 most likely cluster and 10 secondary clusters); from these, two clusters were detected statistically significant [Figure 1]. The first cluster encompasses a wide area of almost the center of the city [Table 1]. In this area, houses are located on the streets of Shariati, Imam Khomeini, Shahid Rajaei, Shahid Beheshti, Shahid Shiroudi, Qaa'em Maqam, Adabjou, Ayatollah Qaffari, and some parts of the Daneshgah avenue. The region has a population of about 131,130, of whom 141 are cases of stomach cancer. The relative risk of this cluster was 1.75 (*P* = 0.01). This cluster is located within a radius of 1.73 km.

The second stomach cancer cluster is in a small area of houses between Taleqani and Shahid Haqqani streets [Table 1] that is in the southwest of Arak. The population of this region is 474, of whom six cases are stomach cancer patients. Relative risk in this cluster was 17.60 (*P* = 0.04). This cluster is located in an area with a radius of approximately 0.085 km.

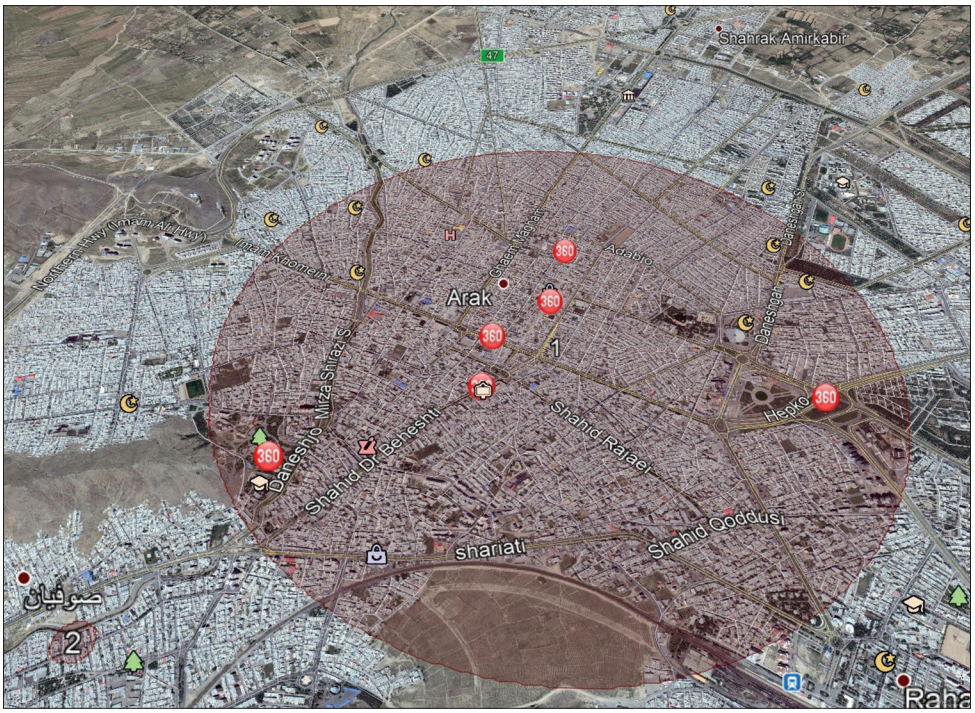

Figure 1: The map of Arak included the significant clusters for stomach cancer from 2009–2014: First cluster (1), second cluster (2)

Table 1: The characteristic of the high-risk clusters of stomach cancer in Arak based on spatial analysis during 2009-2014

Cluster name	Radius	*n* of case	*n* of population	Expected cases	Observed/Expected	Relative risk	*P*
The center of Arak	1.73	141	131130	95.70	1.47	1.75	0.01
Taleghani	0.085	6	474	0.35	17.35	17.60	0.04

Discussion

This study has identified high-risk stomach cancer clusters in Arak from 2009 to 2014. Our results have identified two areas are at a higher risk than others. One of these areas—the first cluster—is a large area in the central part of the city, with a large population. The second identified significant cluster is an area in the southwest of Arak. People living in the second cluster have a moderate to low socioeconomic status that may not have adequate knowledge about the prevention of stomach cancer. These people may also do not have a good lifestyle in terms of risk factors for stomach cancer. People living in the first cluster of the disease are from all different socioeconomic situations. The area is exposed to extensive air pollution due to the high traffic of urban vehicles. To understand the reasons for the difference in clusters in areas with high and low incidence, it is necessary that epidemiological studies be designed on individual and not ecological data. There are also several significant clusters of colorectal cancer in Arak, where the first cluster—the cluster located in the center of the city—has also been formed for colorectal cancer.[17]

Arak is an industrial city with industrial pollutants formed in most months. In Weinmayr *et al*.[6] and Nagel *et al*.,[5] there are some findings on the impact of air pollution on stomach cancer incidence in a cohort study. Weinmayr *et al*.[6] assessed pollutants including copper, iron, and zinc representing nontailpipe traffic emissions; sulphur indicating long-range transport; nickel and vanadium for mixed oil-burning and industry; silicon for crustal material; and potassium for biomass burning. Totally, the association of PM below 2.5 μm of sulphur and stomach cancer was significant. Nagel *et al*.[5] obtained the association between particulate matter (PM) below 2.5 μm and the risk of stomach cancer. Because there is no study to date to identify the air pollution pattern in Arak, it is unknown to state that all of the city is exposed to air pollution. So, it cannot be concluded that the fact could impact in clusters' formation.

Most inhabitants of the central area of Arak seem to be older than the inhabitants in other areas of the city, and since the age range of cancer incidence is higher in older ages, maybe one of the reasons for forming this cluster in the center of the city is the age of people and it is recommended to adjust the analyses for it in subsequent studies. But in general, to understand the reasons for the formation of these clusters, it is necessary to implement epidemiological studies by examining the family history,

the number of years of residence in Arak city as reported in their addresses, nutritional patterns, and other behavioral risk factors. On the other hand, the implementation of ecological studies to analyze the environmental factors related to the risk of stomach cancer in the formed clusters, including exposures to environmental factors and the pollution of drinking water sources, can help clarify the reasons for the formation of these clusters.

Spatial clusters analysis is not only an important tool for disease surveillance and etiology studies, but also effective for health policy making. In fact, the identification of high-risk clusters suggests finding places where people with a stomach cancer live, and this can provide target points for the implementation of educational interventions and screening. In the etiology of stomach cancer, various factors are presented. These include cigarettes,[18-20] red meat,[21] alcohol,[20,21] obesity,[20,22,23] *Helicobacter pylori* infection,[19,20] and consumption of foods containing nitrosamines[21] and high salts.[19,20] Arak drinking water is supplied from Kamal Saleh dam and wells drilled near Arak. Since the amount of nitrate in Arak drinking water is higher than the limit and it seems that such an important finding will be considered in future studies.

This study has strengths and weaknesses. One of the strengths of this study is the use of population-based stomach cancer registries. However, it is necessary to evaluate the sensitivity and specificity of this stomach cancer registration system in future studies. The other strength is the high accuracy in determining the location of the registered addresses of the individuals. As the base unit for the analysis, we have chosen the census block which is the smallest census unit in Iran and the population of each block is determined for it, and in this regard, this analysis is one of the firsts in Arak. This study also has some weak points. There is a probability of misreporting the addresses of the locations where the Information bias may occur.[24,25] On the other hand, a number of registered patients lacked the correct address, and therefore it was not possible to pin point their addresses.[12] So, there may be the possibility of information bias. And since 392 cases of stomach cancer had addresses for analysis, this may lead to insufficient statistical power. There is also the possibility of intraurban migration during the years before the diagnosis of the disease, and we did not consider it in the analysis. This study used the raw population counts without consideration to the age and sex adjustment to identify clusters; this fact was a limitation for this study. On the other hand, in this study, minimum census blocks were applied; for each block, we had only the total population; and we could not access the population by age and sex of blocks, so we used the raw population in each census unit. In general, and given the weak points mentioned, the results of this research should be interpreted with caution.

It is proposed to apply further data about nitrate patterns and other data in the area level to conduct simultaneously ecologic studies.

Conclusions

The findings of this study show that the incidence of stomach cancer is affected by the places. We found two clusters of stomach cancer statistically significant.

In these areas, etiology studies should be conducted at the level of individual data to determine the reason of formation of these clusters. Also, health policies can be implemented in these areas to reduce the risk of stomach cancer. There is a great deal of need for public health programs and the implementation of scientific researches in high-risk areas to find the role of behavioral and ecological factors. However, based on the results of this study, community-based interventions in certain geographical areas can be designed to reduce and control the incidence of stomach cancer.

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Conflicts of interest

There are no conflicts of interest.

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