Original Article

Joint Disease Mapping of Breast, Uterine, and Ovarian Cancers in Cities of Isfahan Province from 2005 to 2010 Using Spatial Shared Component Model

Abstract

Background: Breast, uterine, and ovarian cancers are the most prevalent types of cancers among women. The aim of this study was to estimate the relative risk of these cancers and recognizing spatial patterns of their shared and specific risk factors in cities of Isfahan province, one of the most populated provinces of Iran, using spatial shared component model. **Methods:** In this ecological study, the population consisted of all the registered patients having breast, ovarian, and uterine cancers in the cities of Isfahan from 2005 to 2010. In order to simultaneously analyze these diseases and clarify common and specific patterns of disease, spatial Shared component model was applied. Model fitting was done using Bayesian inference in OpenBUGS software. **Results:** The highest relative risk of breast cancer was seen in Isfahan (4.96), Shahreza (2.37), Dehaghan (5.01), Lenjan (2.33), and Najafabad (2.68), respectively. For ovarian cancer, Isfahan (4.29), Shahreza (2.51), Dehaghan (5.02), Lenjan (2.06), Najafabad (2.00), and Borkhar (2.39) had the highest relative risk, respectively. However, no significant difference was seen among the cities for uterine cancer ($P > 0.05$). **Conclusions:** Since ovarian and uterine cancers are the less prevalent disease in comparison with breast cancer, the preciseness of these estimates were improved remarkably over simple mapping models. Based on this model, the estimates were done according to the correlation between the diseases. After recognizing the spatial patterns of the shared and specific risk factors and reviewing of previous studies, regardless of risk factors data, environmental pollution arises as a potential risk factor.

Keywords: *Breast neoplasms, mapping, ovarian neoplasms, uterine neoplasms*

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Introduction

Malignant breast, uterine, and ovarian cancers are the prevalent diseases among women. Today, over one million women with female-related cancers are known around the world. The most prevalent malignant diseases among females are breast, uterine, and ovarian cancers. In addition, breast cancer is known as the second cause of female death.[1-3] The incidence rate of this cancer is estimated 38 one per 100,000 ones as the commonest cause of female death between 45 and 55 year old ages. The standardized incidences of the mentioned cancer were reported 86.4, and 27.3% in developing countries and developed countries, respectively.[1] Uterine cancer is the third prevalent cancer and one death causes among female around the world. The lead of disease is seen in most countries, so that 86% of reported cases in developing countries.[4] In 2012, 239,000 females suffered from uterine cancer around the world, of which 152,000 of them passed away.[5]

Iran has less incidence of breast cancer in comparison with other countries. However, it has increased in recent years in a way that breast cancer is known as the most prevalent malignancy among Iranian females.[1] Uterine cancer was known as the 10th prevalent cancer (2.8%) among Iranian females in 2010. Ovarian cancer is the eight prevalent cancers and the 12th cause of death in Iran.[6]

In order to also recognize high risk regions and environmental risk factor, different models of disease mapping are used. In fact, disease mapping consists of a series of statistical methods aiming to get precise estimates of incidence rates, disease prevalence and adapt them in the form of

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geographical maps.[7] In recent years, different studies have been conducted about cancer mapping in Iran. However, few of them have focused on joint analysis with emphasis on risk factor roles.[8-10]

Using shared component model (SC), the relative risks of breast, uterine, and ovarian cancers and the effects of shared and specific components of cancers were estimated in Isfahan province from 2005 to 2010 in the form of mapping. Then, the relative importance of the surrogate of the shared risk factor for the mentioned cancers was presented in order to compare the association of the factor with both diseases.

So it can be possible to recognize high and low risk regions for cancers. This information assists health planner in determining the priorities and focusing preventive policies in the known sensitive regions. Also, these findings make it possible to present some hypothesis about possible risk and protective factors specifically and in common for diseases.

Methods

In this ecological study, the studied population consisted of all the registered patients having breast cancer (C52 code in ICD10), ovarian cancer (C56), and uterine cancer (C55) in the cities of Isfahan province from 2005 to 2010. This study was approved with the ethical code IR.MUI.REC.1395.1.131 by Health system research (HSR) of Isfahan University of Medical Science. Spatial shared component model was used with Bayesian inference.

Shared component model

This model analyzes the general risk of three diseases into shared components and three disease-specific components. Shared components are the replacements for unobserved shared risk factors which are justifiable with spatial correlation. Each SC accompanies with scale parameters as the replacement of risk factors. Scale's parameters provide the difference of criterion related to common risk factors for every one of these diseases. Every specific disease represents the unique risk factor of every one of these diseases. They distribute differently rather than other specific disease in spatial level.[11]

According to the following model, the map is divided into n non-overlapped adjacent regions (i = 1, 2, …, n). In addition, k denotes the kth disease (k = 1, 2, …K). Then, θ_{ik}, the relative risk of diseases in i region, is modeled as:

$$O_{ik} \sim Poisson(E_{ik}\theta_{ik})$$

$$\log \theta_{ik} = \alpha_k + \sum_{l=1}^{k} \lambda_{l,i}\delta_{l,k} + \varepsilon_{ik}$$

Where O_{ik} and E_{ik} are the observed and the expected number of cases for k disease in i region. E_{ik} is calculated by multiplying the overall crude incidence rate by the region population. Population of 2006 was used as the year of population statistics.[12]

The disease risk of every one of the mentioned cancers is formulated as below:

$$\log(\theta_{i1}) = \alpha_1 + \lambda_{i1}.\delta_{1,2} + \lambda_{i2}.\delta_{1,3} + \varepsilon_{i1}$$
$$\log(\theta_{i2}) = \alpha_2 + \lambda_{i1}.\delta_{1,2} + \lambda_{i3}.\delta_{2,3} + \varepsilon_{i2}$$
$$\log(\theta_{i3}) = \alpha_3 + \lambda_{i2}.\delta_{1,3} + \lambda_{i3}.\delta_{2,3} + \varepsilon_{i3}$$

θ_{i1}, θ_{i2}, θ_{i3} represent, in turn, related risk of breast, uterine, and ovarian cancers in i number of cities. α_k represents disease-specific intercept of kth cancer. λ_{i1}, λ_{i2}, λ_{i3} represent, in turn, effect of spatial shared components as surrogate of shared risk factors for these three cancers. δ_{i1}, δ_{i2}, δ_{i3} are the scale parameters of the shared risk factors. The estimate of these parameters determines the relative weight of the shared risk factors for the related diseases. ε_{i1}, ε_{i2}, ε_{i3} represent surrogate of specific components as surrogates of specific risk factors for these studied cancers.[13-15] To put it more simply, this model tries to estimate the relative risk of disease to recognize high risky regions, and decompose the risk of diseases to shared and specific effects. According to spatial distribution of shared and specific effects, we emphasize about possible risk factors. It can help politicians to conduct preventive planning in sensitive regions.

The fitting of the models with data was done by use of Bayesian process in OpenBUGS 3.2.1 (rev 781). Posterior distribution estimates for model's parameters was estimated by Monte Carlo Markov Chain methods (MCMC). Brooks-Gelman-Rubin diagnostic tool (BGR) was used in order to test the convergence of all parameters. All the maps were provided using ArcGIS (10.4.1).

Results

Observed and expected cases of breast, uterine, and ovarian cancers in all cities of Isfahan province were shown in Table 1.

Relative risk estimates of cancers

Using the spatial shared component (SC) model, the relative risk of every studied cancer were estimated in a 6-year period. The achieved geographical distribution is shown in Figure 1. All maps were numbered based on codes of Table 1. Also, the distribution of estimating shared and specific effect of the mentioned cancers was illustrated. The results show the following points, whereas relative risks and their Bayesian confidence intervals (BCI) are shown in parentheses:

- **Breast cancer**: Isfahan [4.96; (3.19, 7.56)], Shahreza [2.37; (1.47, 3.72)], Dehaghan [5.01; (2.09, 9.85)], Lenjan [2.33; (1.47, 3.64)], Najafabad [2.68; (1.70, 4.13)], and Fereidan [1.67; (1.00, 2.74)] had the highest relative risk. In contrast, Aran & Bidgol [0.18; (0.06, 0.40)], Kashan [0.11; (0.05, 0.21)],

Tiran & Karvan [0.38; (0.16, 0.72)], and Khansar [0.43; (0.14, 0.93)] had the least relative with respect to the other cities

- **Uterine cancer**: No significant difference was found among the cities ($P > 0.05$)
- **Ovarian cancer**: Isfahan [4.29; (2.68, 6.79)], Shahreza [2.51; (1.35, 4.37)], Dehaghan [5.02; (1.64, 12.32), Lenjan (2.06; (1.14, 3.48)], Najafabad [2.00; (1.12, 3.35)], Fereidan [1.89; (0.99, 3.51)], Borkhar [2.39; (1.29, 4.14)], and Fereidoonshahr [1.69; (0.71, 3.68)] had the highest relative risk. Aran & Bidgol [0.21; (0.05, 0.51)], Kashan [0.14; (0.04, 0.32)], Tiran & Karvan [0.41; (0.14, 0.86)], and also Natanz [0.32; (0.09, 0.76)] had the lowest levels of relative risk with respect to the other other province's cities.

Table 1: Observed and Expected cases of breast, uterine and ovarian cancers in cities of Isfahan province from 2005-2010

Code	Cities	Breast cancer		Uterine cancer		Ovarian cancer	
		O_i	E_i	O_i	E_i	O_i	E_i
1	Semirom	9	66.03	0	0.87	7	7.98
2	Aran & Bidgol	4	75.14	1	0.99	0	9.08
3	Ardestan	19	39.77	0	0.52	2	4.81
4	Isfahan	2662	1604.69	25	21.09	323	194.00
5	Borkhar	128	125.57	2	1.65	14	15.18
6	Tiran & Karvan	8	62.60	0	0.82	0	7.57
7	Khomeinishahr	143	222.83	6	2.93	14	26.94
8	Khansar	3	28.71	0	0.38	1	3.47
9	Dehaghan	9	4.50	0	0.06	1	0.54
10	Shahinshahr and Meymeh	109	176.69	2	2.32	5	21.36
11	Shahreza	93	116.94	1	1.54	14	14.14
12	Fereidan	43	78.73	1	1.03	9	9.52
13	Fereidoonshahr	14	38.00	2	0.50	5	4.59
14	Falavarjan	114	202.64	2	2.66	14	24.50
15	Kashan	8	243.03	1	3.19	1	29.38
16	Lenjan	147	187.27	3	2.46	18	22.64
17	Mobarakeh	38	111.04	1	1.46	8	13.42
18	Naein	9	48.69	0	0.64	0	5.89
19	Najafabad	208	228.92	2	3.01	19	27.67
20	Natanz	2	38.78	0	0.51	1	4.69
21	Chadegan	5	33.43	0	0.44	1	4.04
22	Golpayegan	30	71.02	1	0.93	3	8.59

Estimate of shared component factor of cancers

The regions that have higher risk of the shared risk factor of breast and ovarian cancers were the central regions of province including Isfahan, Borkhar, Shahreza, Dehaghan, Najafabad, Lenjan, and Khansar. No significant difference was found for two other shared components' distribution.

The relative importance of shared risk factor component for cancers

Table 2 represents the posterior medians for scale parameters. These parameters determine the relative weight of the shared risk factors for the related diseases. According to their Bayesian confidence intervals, none of them were significant.

Estimate of surrogate of specific risk factor components

- **Breast cancer**: Isfahan, Naein, Ardestan, Natanz, Borkhar, Shahinshahr, Meymeh, Golpayegan, Najafabad, Tiran & Karvan, Khomeinishahr, Lenjan, Dehaghan, and Shahreza exposed more to specific risk factor of breast cancer
- **Uterine cancer**: Naein, Isfahan, Borkhar, Shahinshahr and Meymeh, Golpayegan, Khansar, Fereidan, Fereidoonshahr, Chadegan, Khomeinishahr, Falavarjan, Lenjan, Mobarakeh, Dehaghan, Aran & Bidgol, and Shahreza were more exposed to specific risk factor of Uterine cancer
- **Ovarian cancer**: Isfahan, Felavarjan, Lenjan, Mobarakeh, Khansar, Semirom, Chadegan, Fereidan, Fereidoonshahr, Shahreza, and Dehaghan were more exposed to specific risk factor for ovarian cancer.

Discussion

Using SC, spatial distribution of relative risk related to breast, uterine, and ovarian among cities of Isfahan province was estimated and the shared and specific components of these cancers were recognized. This can lead to provide some hypothesis regarding risk and protective specifically and in common with the diseases.

The relative risk of breast cancer incidence was higher in Isfahan, Shahreza, Dehaghan, Lenjan, Najafabad, and

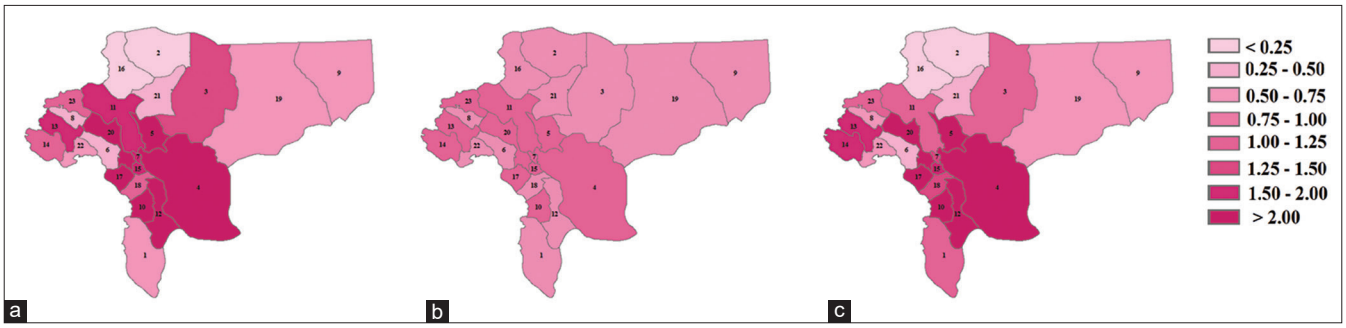

Figure 1: Maps of the estimated relative risk of (a) breast, (b) uterine, (c) ovarian cancers in Isfahan cities from 2005 to 2010, based on SC Model

Fereidan rather than other cities. The studies show that Isfahan province has the highest incidence of breast cancer in the country.[15-18] However, no studies were conducted yet in Isfahan cities to recognize the spatial pattern.

Relative risk distribution of ovarian cancer is the same as breast cancer. The investigation showed that Isfahan province has one of the highest ovarian cancer incidences in the country.[17-19] Relative risk estimation of uterine cancer seems to be the same in all cities. However, no studies have been done to assess incidence rates or risk of this disease in this province. The map of Figure 2a-c shows spatial distribution of estimating cancer's shared risk factors. This model of breast and ovarian cancers are so similar to the relative risk model of every one of these cancers. The risk was reduced in cities far away from the center of province. Shared component patterns of breast and uterine cancers and also uterine and ovarian cancers show no important differences among the cities.

The map of Figure 2d-f shows cancer's specific component distribution. The severity of these factors in every map is approximately the same.

Some investigations indicate to Pb (lead) role in developing breast cancer tumors.[20] Rashidi has found that the distribution of common malignancies such as breast cancer are so similar to the map of geographical pattern of soil Pb in Isfahan.[21] Amini studied the pollution of soil to Pb in Isfahan province. He found that exposed soils were polluted by this element in Isfahan city. Using petrol contained lead, composite in city parks and mine extractions lead to increase the concentration of Pb (lead) remarkably in the soil.[22]

Moradi investigated the incidence patterns of ovarian cancers in Iran. Isfahan province is one of regions in which this cancer has been developed increasingly. In this study, obesity, smoking, inactivity, inappropriate nutrition, early menarche, and late menopause were known as the risk factors of ovarian cancer.[19]

Over 95% of uterine cancers' are caused by Human Papilloma Virus (HPV) infection.[23,24] Mirzaei Kashani studied uterine cancer patients in Isfahan to estimate the incidence of HPV infection. He found that the rate of HPV infection in chronic cases of uterine cancer has increased.[25]

Awareness of the spatial distribution of relative risk of cancers as well, their shared and specific risk factors can help politicians to recognize the high risky regions and proceed the prevention policies. Also, this study will serve as a base for future studies to assess association between the incidence of mentioned cancer and the suggested risk factors in sensitive regions.

Table 2: Posterior Median and 95% BCI*s for relative weight of shared risk factor (δ)

Cancers	Median		
	Breast and ovarian	Breast and uterine	Ovarian and uterine
Breast cancer	1.059 (0.8392-1.286)	1.115 (0.4837-2.233)	
Uterine cancer		0.896 (0.447-2.067)	0.880 (0.437-2.080)
Ovarian cancer	0.944 (0.777-1.191)		1.136 (0.4806-2.287)

*Bayesian Confidence Interval

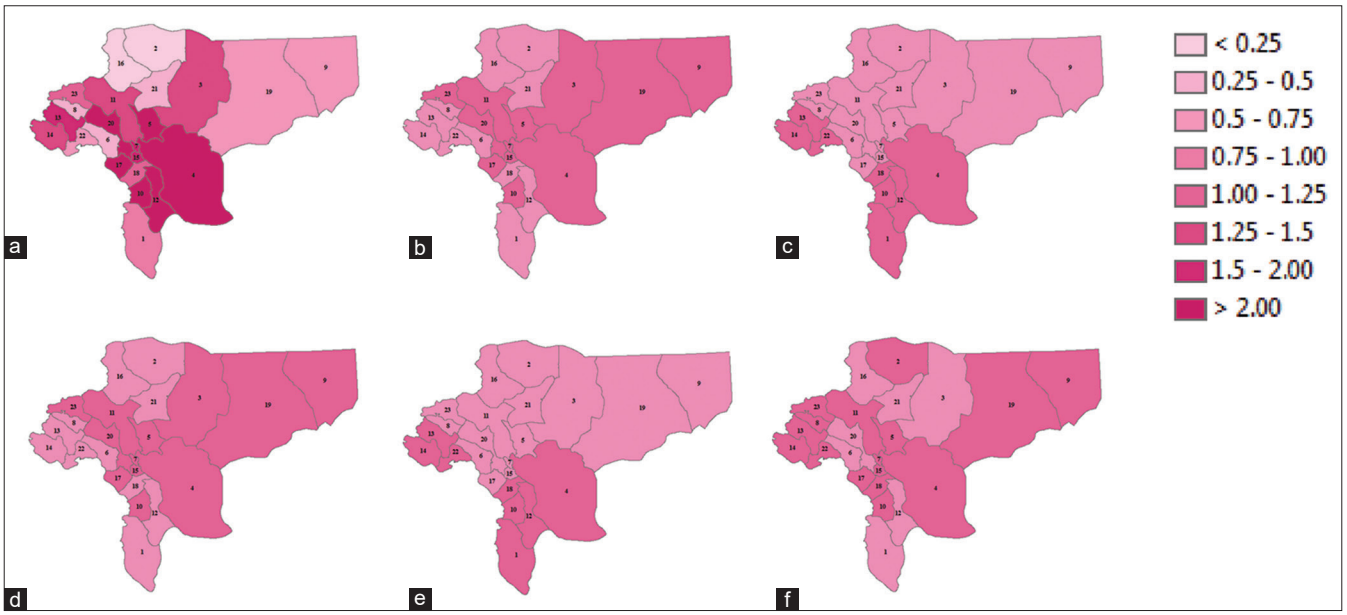

Figure 2: Maps of the surrogate component of the shared risk factor of (a) breast and ovarian, (b) breast and uterine, (c) ovarian and uterine cancers; and the surrogate components of specific risk factors of (d) breast, (e) ovarian, (f) uterine cancers

However, our study has several limitations. The study is limited in having a province of Iran, and the findings clearly cannot be extrapolated to whole of Iran. The results are not used in personal level because of ecological bias, but they can be followed as an appropriate goal to find the causes and make. Seeing that, this model is disregarding surrogate of shared risk factor component in triple disease from in SC. This can be modified by using polytomous logit (PL) model.[26] Since all cancer cases are not registered completely in Iranian nation-wide system, it is possible to lose some cases in some cities and in the first years of study process due to inefficient knowledge and facilities.

It is suggested to apply the spatio-temporal SC model to achieve accurate spatial models with respect to time dimension, and determine the temporal trend of relative risk of diseases.[27] If recent information and different age groups become provided, valuable results of disease process and mark high risky population would be available for policy-makers of control, prevention, and treatment fields of moment's cancers. In order to overcome ecological bias, it is recommended to use multilevel models and regard individual level in the form of nest in geographical levels. This is done to study the association between risk factors and relative risk roles of cancers incidence.

Conclusions

The main conclusion to be drawn from this discussion is that the best way to make awareness of the spatial distribution of relative risk of cancers as well, their shared and specific risk factors, when we do not have access to original information of the risk factors is using SC model. On balance, considering environment health and controlling environmental pollution performing screening program and educational cancers in large scales can lead to increase women's knowledge toward early diagnosis methods of breast and ovarian cancers and transmitting ways of HPV. They are all known as control and preventive alternatives of cancers.

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Conflicts of interest

There are no conflicts of interest.

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