

## The Geographical Clusters of Gastrointestinal Tract Cancer in Fars Province, Southern Iran

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### ABSTRACT

**Background:** Gastrointestinal tract cancer (G.I.C) is one of the common cancers in world-wide. The incidence rate of it is different in various geographical regions. This study was performed to assess spatial clusters of the occurrence of G.I.C in Fars Province.

**Methods:** In this cross-sectional study, the new cases were 4569 cases from 2001 to 2009. The crude incidence rates were standardized based on world population for both sexes. The spatial analysis was conducted using the geographical information systems. We used the local Indicators of spatial association measure, in order to identify local spatial clusters.

**Results:** From a total of the new cases, 62.8% cases were male. The most common G.I.Cs were stomach and colorectal cancer in men and women respectively. The significant cluster patterns were discovered from 2002 to 2007. The common type of spatial clustering was a high-high cluster, that to indicate from North-west to South-east of Fars Province.

**Conclusions:** Analysis of the geographical distribution of G.I.C will provide opportunities for policymakers for applying preventive measures. Furthermore, it could be helpful for researchers for future epidemiological studies for investigation of etiological agents in regions with significant spatial clustering of high incidence of cancer.

**Keywords:** Gastrointestinal neoplasm, Iran, spatial clustering

### INTRODUCTION

Cancer has affected increasingly the human population during the past decades. In the less developed and economically transitioning countries burden of cancer is increased due to adoption of unhealthy western life-styles such as smoking, physical inactivity and caloriendense food.<sup>[1]</sup> Cancer is the third most common cause of death in Iran after cardiovascular diseases and car accidents.<sup>[2-4]</sup> In the Eastern Mediterranean region of World Health Organization, Iran is the second country in cancer mortality rate.<sup>[5]</sup>

Gastrointestinal tract cancer (G.I.C) is one of the common cancers in the world-wide.<sup>[6]</sup> The burden of G.I.C is heavy for patients with gastrointestinal disease, because it is the major cause of mortality and hospital admissions. Furthermore, increase in the incidence of

most gastrointestinal diseases has major implications for health care systems and health communities.<sup>[7]</sup>

The incidence rate of GI.C is high in Iran as well as the less developed countries.<sup>[8]</sup> Annually about 50,000 new cases of cancer are reported in the country and hence that in almost 38% of the cases, the GI.C is partially affected.<sup>[6,9]</sup> GI.C have been observed as one of the most common fatal cancer in Iran.<sup>[9]</sup> It is related to diagnosis at advanced stages and inequality in access to effective therapies. So early detection may increase the chance of successful treatment and decrease the burden of cancer.<sup>[9,10]</sup>

GI.C incidence is different in the various Provinces of Iran. The northern part of the country is well-recognized to be the region with the highest incidence of the GI.C.<sup>[11]</sup> The geographical distribution of cancer especially GI.C suggests a relationship between its occurrence and the environment such as ecological cultural, genetic and socioeconomic factors.<sup>[4,5,10,12]</sup>

The spatial analysis of cancer rate is effectively communicated among policymakers and public health researchers. The mapping of health statistics can show occurrence rates in certain areas, geographic trends and allow comparison of disease patterns with patterns of risk factors.<sup>[13]</sup>

In Iran, most of the existing literature in this context is on epidemiological studies that have not used spatial statistics by a geographical information system (GIS).<sup>[2,4,11,14]</sup>

Despite variations in incidence, however, a few studies have documented evaluation of geographical variation of GI.C incidence by applying GIS.<sup>[9,15]</sup>

The purpose of the present paper is to describe the incidence of GI.C and geographical differences in its incidence in the various parts of Fars Province using GIS during the years 2001-2009.

## METHODS

This study was carried out in Fars Province, which is located in southern Iran and has an area of about 122,400 km<sup>2</sup> and is located at 27°31'-31°42' longitude North and 50°37'-55°38' latitude East.<sup>[16]</sup> The total population of Fars is about 4.6 million and male to female ratio is 1.03.<sup>[17]</sup> The administrative divisions in 2010 included 24 counties. The capital city is Shiraz, one of the metropolises in Iran [Figure 1].

In this cross-sectional study, the major sources of data collection related to cancer were derived from the Cancer Registry Center of Shiraz

University of Medical Sciences, which covers the population of Fars. The cancer data were reports from hospitals and diagnostic departments based on histopathological findings from 2001 to 2009. GI.C is a term that encompasses a group of cancers that affect the gastrointestinal tract. Types of GI.Cs include esophagus, stomach, small intestine, colon and rectum, anus, liver, bile ducts, gall bladder and pancreas.<sup>[18]</sup>

The data sheet included 33,398 patient names, sex, age at the time of diagnosis, place of residence and cancer diagnose and was based on the international classification of disease for oncology.<sup>[19]</sup> The data were checked and any duplicates cases with the same information, cases from other provinces, diagnosis other than GI.C and uncertain addresses were excluded. The final data were summarized in another sheet and included 4569 new cases and consisted of sex, place of residence and an eight age-group classification.

The crude incidence rates were calculated in various age groups and for both genders in each county of the province Fars every year. In order to control age as a confounding variable, we computed age-standardized incidence rates (ASRs) per 100,000 persons using the direct method of standardization to world population.<sup>[20]</sup>

The calculated ASRs were transferred to the GIS software (Arc GIS 9.3) and the mapping tools of GIS were used for visualizing ASR for each year. In GIS, various types of maps could commonly be used for health statistics. We applied a graduated scale referred to in the software (graduated symbol) in percentage of total ASR of each year. The classification was manually constructed in five



**Figure 1:** Map of counties of Fars

classes and then applied to maps in each series. Furthermore, we used exploratory spatial data analysis (ESDA) to determine the distribution pattern of cancer for each year. Moran's index was applied as a useful measure of spatial autocorrelation for detecting spatial clusters. This index shows the degree of association of a variable in relation to its location, to refer similarity between neighboring observations in a pattern. The null hypothesis is that there is no spatial autocorrelation or significant clustering among ASR in the counties. Whereas the alternative hypothesis suggests that a significant clustering exists. Moran's index is tested by computing standard normal deviate (Z score) and to take values in the range (-1, 1). A significant positive autocorrelation coefficient, indicates clustering i.e. when nearby regions are similar in ASR. Clustering pattern for counties can be high-high, low-low, high-low or low-high level in comparison to their neighboring counties. The first two categories indicate the expected spatial clustering, where regions with similar features tend to be closer to each other. High-low or low-high level, however are considered as spatial outliers. If Moran's index is a significant negative value, that counties are dissimilar and there is no clustering. A Moran's index of approximately zero shows that the distribution pattern is randomly.<sup>[21,22]</sup>

We used the local indicators of spatial association (LISA) measure to identify local spatial clusters. LISA analysis was generally mapped to indicate counties with high Moran's index coefficient, which suggested clusters of similar values among various regions.<sup>[21]</sup> ASR calculation was performed in Microsoft Excel and spatial and temporal analyses were performed using Arc GIS 9.3™ and Geoda 1.0.1™.

## RESULTS

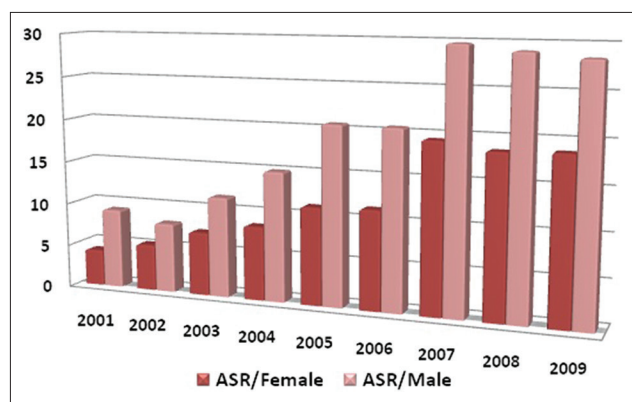
A total of 4569 new GI.C cases were diagnosed during 2001-2009 in Fars Province, that 2870 (62.81%) cases were male. The mean ages were approximately  $69.93 \pm 1.3$  years and  $64.95 \pm 1.5$  years for men and women, respectively. ASR of GI.C as shown in Figure 2 that the highest ASR was due to 2007. The average ASRs were 19.15 and 11.67/100,000 persons in men and women, respectively.

Table 1 shows the population of each county during Fars in 2001-2009 and the values of ASR for each year of the study period.

Table 2 and Table 3 show the principle GI.C sites in each sex. According to ASR, the most common cancer in men was stomach cancer (85.04) and among women it was colorectal cancer (48.15). For mapping of GI.C, total ASR distribution of regions is plotted in Figure 3. In the most of the counties, ASR for men was observed more than women. The distribution pattern of cancer was dispersed, but in the last few years in the period, scattering was less and the proportion of each county was increased. Approximately, it was up to 0.5% in 2008 and 2009. High incidences occurred in the most of the northern counties and some of the southern counties (Larestan, Lamerd and Darab) [Figure 3].

By using ESDA, clustering patterns were discovered from 2002 to 2007 and hence that Moran's index was significant in these years [Table 4].

Geoda Software was utilized to determine spatial clusters in certain years. Figure 4 is a LISA map that shows the four spatial clustering types. The red counties represent high ASR are surrounded by those which also have high ASR. The high-high cluster is concentrated on Shiraz, Sepidan, Mamasani, Nayriz, Estahban, Fasa, Firuzabad and Kazerun. The high-low cluster (Larestan) indicates that it has a high ASR in contrast with its neighboring counties [Figure 4]. In the first 5 years, occurrence of cancer in men was dispersed in the counties and then gradually, ASR became less scattered and proportion of counties in 2007-2009 period increased in the smoothed maps [Figure 5]. The spatial dependency of cancer was clustered in 2003-2006 and 2009 at the significance level of 0.05 for men [Table 4]. The distribution map of ASR of women was approximately scattered



**Figure 2:** The age standardized rate in Fars Province, Iran, 2001-2009

**Table 1:** ASR of G.I.C in counties of Fars Province, Iran, during 2001-2009

County	Mean of population (2001-2009)	Total ASR								
		2001	2002	2003	2004	2005	2006	2007	2008	2009
Abadeh	92210	7.14	6.32	3.58	5.87	6.60	13.37	10.48	11.10	36.45
Arsanjan	41875	0.00	7.89	3.93	7.52	20.81	0.00	16.39	1.44	28.05
Bavanat	46262	2.38	1.84	4.03	8.18	1.28	2.44	11.53	15.76	14.40
Darab	174971	9.53	5.35	9.65	19.69	13.04	15.65	11.01	28.66	23.91
Eqlid	103965	3.38	0.00	6.19	13.99	10.71	5.58	14.73	26.97	19.27
Estahban	67206	0.00	3.55	4.08	9.95	9.60	20.41	16.55	11.86	11.27
Farashband	44582	0.00	2.81	7.85	3.37	3.48	5.66	35.72	12.32	7.99
Fasa	191550	0.76	3.95	3.86	7.80	18.79	23.93	24.12	7.89	14.95
Firuzabad	114841	9.11	11.45	16.80	11.84	23.87	22.50	37.32	19.91	17.68
Jahrom	201115	4.61	4.05	6.00	3.12	6.85	16.27	19.15	11.88	9.20
Kazerun	265649	6.50	3.21	11.37	13.67	15.17	12.78	25.57	19.12	14.11
Khonj	39416	0.00	0.00	0.00	0.00	0.00	0.00	7.23	4.59	7.38
Khorrambid	44632	0.00	4.27	0.00	3.23	3.25	3.27	8.19	24.03	13.87
Lamerd	77210	7.56	1.43	10.01	6.87	4.57	1.23	13.05	16.51	1.60
Larestan	226197	5.37	4.27	8.34	8.10	14.05	13.76	18.11	20.79	18.13
Mamasani	165254	5.05	8.20	13.51	14.22	12.69	11.21	21.34	20.93	20.16
Marvdasht	293994	7.04	4.68	10.41	10.92	18.52	16.72	27.04	23.16	22.19
Mohr	53488	0.00	0.00	3.17	3.86	0.00	0.00	2.92	0.00	16.88
Nayriz	106335	9.49	5.55	8.04	12.91	11.97	8.89	18.92	18.32	16.55
Pasargad	30304	7.39	0.00	0.00	0.00	0.00	0.00	10.49	13.14	22.59
Qir and Karzin	63969	0.00	2.51	6.80	1.61	10.33	4.27	0.00	0.00	5.07
Sepidan	89510	5.00	10.75	12.54	18.07	7.75	17.67	24.92	18.30	14.70
Shiraz	1679605	9.65	9.49	12.09	15.25	22.35	20.93	32.77	33.74	33.49
ZarrinDasht	62351	0.00	0.00	3.08	0.00	2.43	0.00	0.00	7.26	6.97

ASR=Age standardized incidence rate; G.I.C=Gastrointestinal tract cancer

**Table 2:** Age-specific incidence rates, crude incidence rate and ASR of G.I.C (2001-2009) in men, Fars Province of Iran

Sites	No.	0-20	21-34	35-44	45-54	55-64	65-74	75-84	≥85	Crude	ASR
Esophagus	308	0/11	1/29	3/76	25/37	87/48	113/35	316/94	428/61	15/26	23/13
Stomach	1171	0/55	4/81	30/52	115/56	272/53	484/19	1131/91	879/78	58/00	85/04
Colon and rectum	889	0/77	7/39	40/56	118/38	219/82	282/68	675/03	338/38	44/04	63/36
Liver	179	0/88	1/48	3/76	21/84	43/74	50/38	181/11	90/23	8/87	12/72
Gallbladder, etc	103	0/00	0/37	2/09	10/57	19/07	41/98	123/48	90/23	5/10	7/42
Pancreas	113	0/00	1/29	2/09	13/39	25/80	48/98	78/20	112/79	5/60	8/26
Other G.I.C	107	0/44	1/85	5/02	12/68	16/82	29/39	82/32	157/91	5/30	7/42
Total	2870	3/64	22/18	101/19	369/24	772/73	1291/63	2975/90	2165/60	142/16	240/96

ASR=Age standardized incidence rate; G.I.C=Gastrointestinal tract cancer

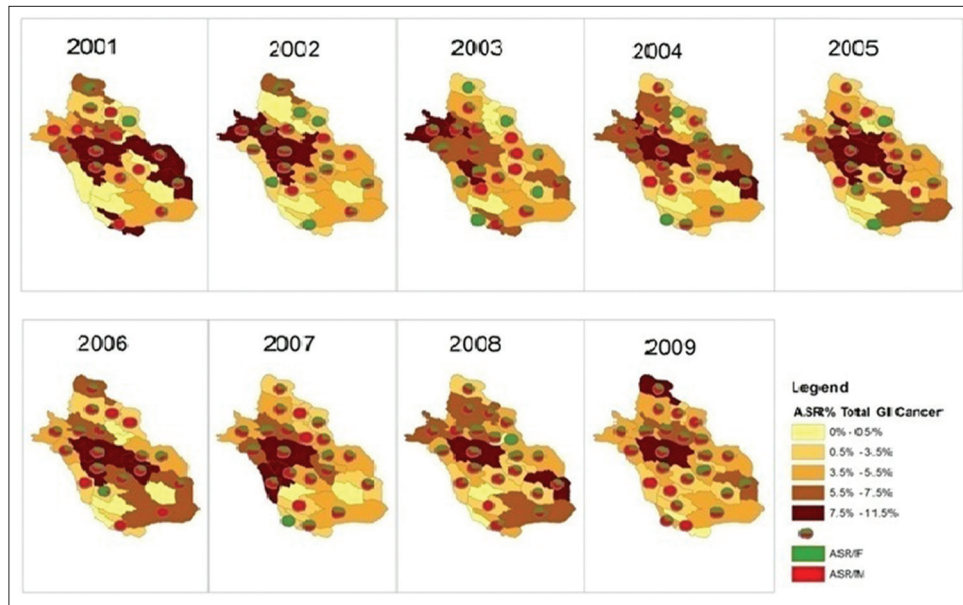
in the period of study. Most of northern counties of Fars had a regular and increasing trend, but southern counties did not and to move revealed and increasing pattern of ASR in the final years (2007-2009). The geographical distribution was random in most years and showed significant spatial autocorrelations and clustering only in the 2003, 2004 and 2007 [Figure 6].

## DISCUSSION

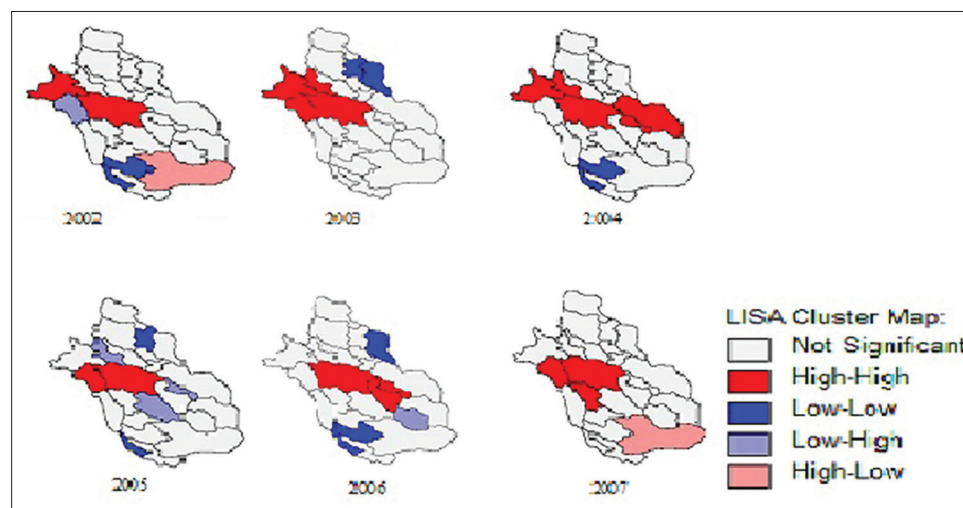
Whereas epidemiology of cancer incidence using GIS has been well-studied in developed countries, it has not received adequate attention in developing countries.

As, there are not enough study about mapping G.I.C in different parts of Iran, especially from southern Provinces, we compared findings based





**Figure 3:** Spatial distribution of gastrointestinal cancer in the counties of Fars, during 2001-2009



**Figure 4:** Spatial clusters of total of age standardized incidence rate in Fars Province, 2001-2009

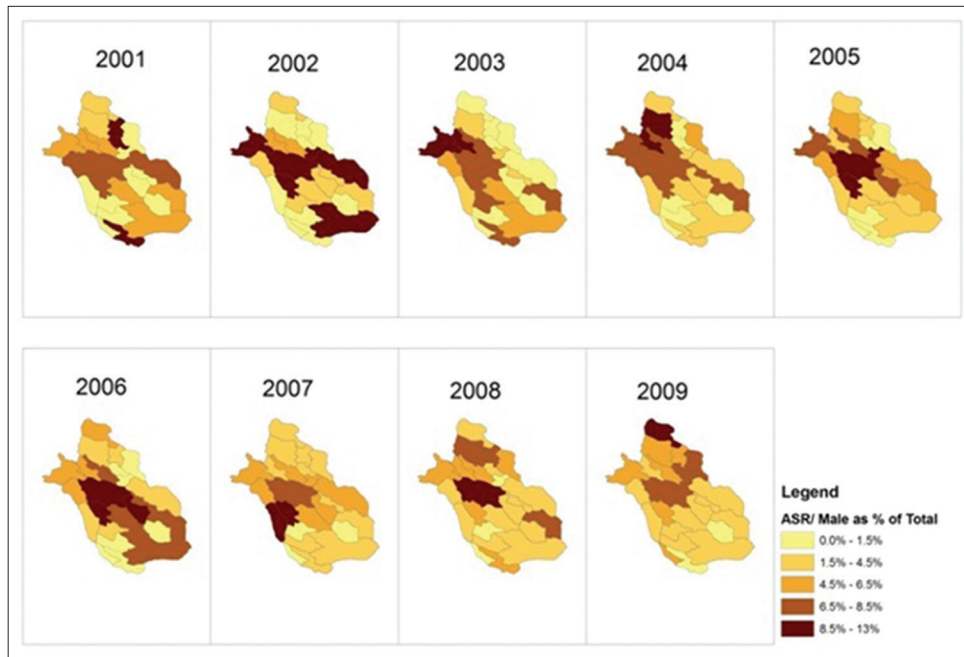
**Table 3:** Age-specific incidence rates, crude incidence rate and ASR of GI.C (2001-2009) in women, Fars Province of Iran

Sites	No.	0-20	21-34	35-44	45-54	55-64	65-74	75-84	≥85	Crude	ASR
Esophagus	166	0/11	2/78	9/59	28/79	57/03	53/67	22/57	118/65	8/48	13/15
Stomach	494	0/46	5/56	21/80	57/58	114/06	208/16	424/36	135/60	25/24	36/93
Colon and rectum	642	0/92	7/04	33/14	98/31	162/94	235/81	379/21	186/45	32/81	48/15
Liver	152	0/92	2/04	8/29	17/56	26/77	52/04	135/43	67/80	7/77	10/86
Gallbladder, etc.,	117	0/11	0/19	3/92	11/94	31/42	48/79	135/43	33/90	5/98	9/03
Pancreas	66	0/00	0/74	1/74	7/02	20/95	26/02	58/69	16/95	3/37	5/09
Other GI.C	62	0/23	1/67	2/62	7/72	16/29	19/52	27/09	33/90	3/17	4/48
Total	1699	3/33	20/37	93/76	247/89	485/33	832/66	1431/08	661/05	86/82	149/57

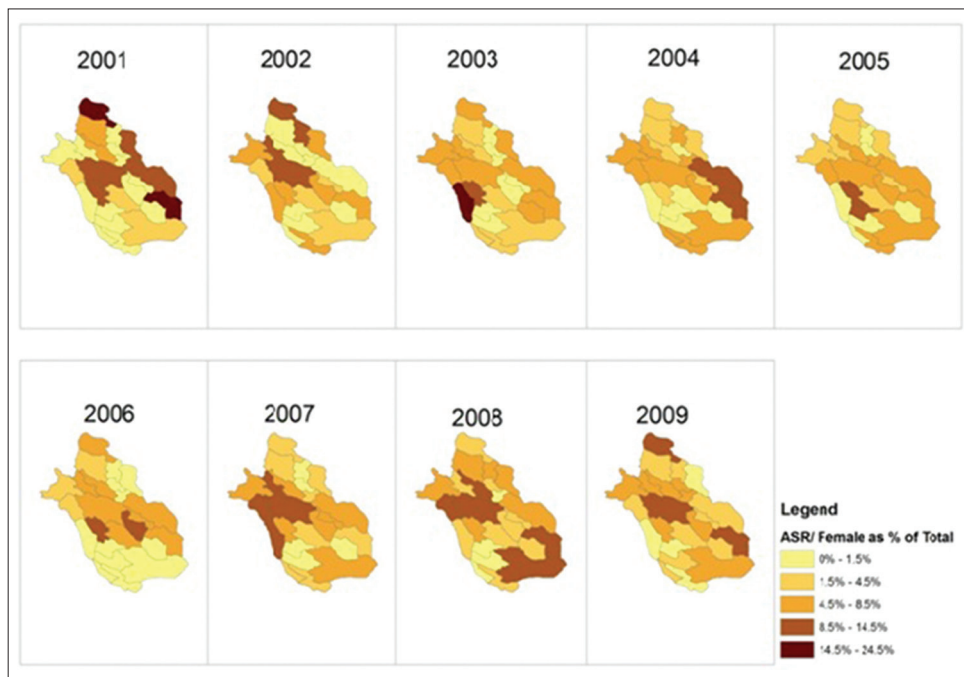
ASR=Age standardized incidence rate; GI.C=Gastrointestinal tract cancer

on epidemiologic aspects of GI.C in our study. The total ASRs were 240.96 and 149.57 among men

and women respectively. In contrast of the findings of Mehrabani *et al.*, (9.14, 5.9) and Masoompour



**Figure 5:** Spatial distribution of gastrointestinal cancer in men, during 2001-2009



**Figure 6:** Spatial distribution of gastrointestinal cancer in women, during 2001-2009

*et al.*, (20.1 and 12.4), our results showed an increased incidence.<sup>[4,14]</sup> This increasing trend of GI.C in may be due to improvements in cancer registry, diagnostic facilities, aging of the population and non-correct westernized lifestyle.<sup>[23]</sup>

The Northern Provinces of Iran are well known with high GI.C ASR in the world. Hossein Somi

*et al.* have reported ASR 40.4 and 26.1 in men and women respectively in East Azerbaijan. Furthermore the mean age at the time of first diagnosis was lower than our study.<sup>[11]</sup> The study has conducted by Mohebbi *et al.* in 2001-2005 in Mazandaran and Golestan provinces of Iran found very high of ASRs (51.8 for men, 33.4 for women).<sup>[9]</sup>

**Table 4:** Indices of spatial autocorrelation GI.C during 2001-2009

Year	Sex	Moran's index	Z score	P value	Type of spatial pattern	ASR
2001	B	-0.065	-0.180	0.857	Random	6.79
	M	-0.076	-0.275	0.783	Random	9.25
	F	-0.066	-0.197	0.844	Random	4.20
2002	B	0.210	2.163	0.031	Clustered	6.78
	M	0.117	1.356	0.175	Random	8.06
	F	-0.085	-0.356	0.722	Random	5.37
2003	B	0.295	2.872	0.004	Clustered	9.58
	M	0.231	2.287	0.022	Clustered	11.61
	F	0.144	1.665	0.096	Clustered	7.35
2004	B	0.291	2.820	0.005	Clustered	11.93
	M	0.265	2.579	0.010	Clustered	15.01
	F	0.152	1.688	0.091	Clustered	8.56
2005	B	0.234	2.338	0.019	Clustered	16.04
	M	0.276	2.702	0.007	Clustered	20.65
	F	0.107	1.280	0.201	Random	11.28
2006	B	0.347	3.262	0.001	Clustered	16.03
	M	0.274	2.656	0.008	Clustered	20.58
	F	0.079	1.265	0.206	Random	11.46
2007	B	0.194	2.022	0.043	Clustered	24.68
	M	0.103	1.289	0.197	Random	29.71
	F	0.253	2.489	0.013	Clustered	19.45
2008	B	0.042	0.729	0.466	Random	23.79
	M	-0.035	0.071	0.944	Random	29.01
	F	0.098	1.191	0.234	Random	18.58
2009	B	0.145	1.628	0.103	Random	23.62
	M	0.265	2.667	0.008	Clustered	28.44
	F	0.146	1.598	0.110	Random	18.77

ASR=Age standardized incidence rate; GI.C=Gastrointestinal tract cancer; B=Both; M=Male; F=Female.  $P=0.05$

In our study, the most common of GI.C in men and women was stomach and colorectal cancer respectively, as well as other provinces of Iran and less developed countries,<sup>[2,11,15]</sup> in contrast East Azerbaijan, Mazandaran and Golestan provinces, the esophagus cancer was common in women.<sup>[11,9]</sup>

According to the findings of Mehrabani *et al.* in Fars, ASR of stomach cancer in men was 3.82 and colorectal cancer in women was 2.41, whereas we found higher significantly [Tables 2 and 3].<sup>[4]</sup> The stomach cancer may be related to high prevalence of *Helicobacter pylori* infection, genetic factors, change of diet and smoking.<sup>[5,24]</sup> The colorectal cancer was the most frequencies in women, that may be associated with consuming high calories,

low-fiber diet and high body mass index especially in women.<sup>[14]</sup>

The assessment of spatial distribution of GI.C by ESDA, the obtained Moran index shows that geographical clusters in the men were similar to total ASR. But the Moran's index of ASR in women were less clustering patterns in the time of the study. It may be loss of regularity incidence and not completing correct address of residence.

From the four types of spatial clustering, the high-high clusters were important and to be observed on the Shiraz, Sepidan, Kazerun, Mamasani, Estahban, Fasa, Firuzabad, Nayriz and Jahrom. Probably, there are common risk factors that to induce high incidence of GI.C in these counties.

This study showed a presentation of the distribution of GI.C on the maps using GIS. GIS is utilized as effective technology to determine the health maps and significant clusters, that it can help to policymakers and researchers in order to decision making for the further studies in geographic areas with clusters of high cancer incidence.<sup>[25]</sup> The researchers should consider not only maps help to visually evaluate geographical pattern, also the significant clusters were the golden points for epidemiological studies. Therefore the cancer registry should be accurate, clear and residence address for GIS researchers.

## CONCLUSIONS

The GIS analysis is a method that is feasible and helpful in generating hypothesis and identifying areas for intervention. It could be necessary and important to help researchers to assess risk factors. Therefore, knowledge of geographical distribution of cancer is expected to provide accurate and easily accessible information for implementation of preventive activities in community health.

Further studies are needed on the efficiency of GIS, not only to determine etiological agents of cancer but also to help policy makers in management of health promotion and preventive strategies.

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