

## RESEARCH ARTICLE

# Trend Analysis of Gastrointestinal Cancer Incidences in Guilan Province: Comparing Rates over 15 Years

Zahra Atrkar-Roushan<sup>1</sup>, Anoshirvan Kazemnejad<sup>2\*</sup>, Fariborz Mansour-Ghanaei<sup>3\*</sup>, Farid Zayeri<sup>4</sup>

### Abstract

**Background:** Cancers of gastric and esophagus are the most frequent gastrointestinal (GI) tract cancers in Iran. This study aimed to analyze time trends of GI tract cancers in Guilan province by gender and age to provide solid scientific evidence for cancer prevention and control. **Materials and Methods:** The data were obtained from the Guilan Cancer Registry System and Guilan Provincial Health Center, over the 15 year period between 1997 and 2011. Crude incidence and age standardized (AS) incidence rates were calculated and annual percent change was estimated by Joinpoint software for long term trend analysis. **Results:** During the study period, 8,332 cases of GI malignancies with a male to female ratio of 1:1.73 were registered in Guilan province. The AS rates for esophageal, gastric, colon and rectal cancers were 5.97, 14.5, 7.59 and 3.58 per 10<sup>5</sup> respectively. While the trend was declining and relatively constant for esophageal and gastric cancer, respectively, the incidence trend for colon and rectal cancers was of increase over the period of the study. **Conclusions:** The results indicated that the incidence of GI cancers was relatively low in Guilan province compared to neighboring provinces. An effective cancer control program including prevention measures, early detection and effective treatment needs to be implemented to reduce cancer morbidity and mortality.

**Keywords:** Trends - gastrointestinal cancers - AS incidence rates - Guilan province - Iran

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### Introduction

Cancer is a major public health concern in the world and one of the 5 leading causes of death in all age groups in males and females (Herszenyi and Tulassay, 2010). Based on the GLOBOCAN 2008 estimation, approximating 12.7 million cancer cases and 7.6 million cancer deaths occurred in 2008; of these, 56% of the cancer cases and 64% of the cancer related deaths happened in the developing countries (Jemal et al., 2011). Cancer is the third most common cause of death in Iran (Pourhoseingholi et al., 2009). The global burden of cancer continues to increase largely because of the aging of the world population, alongside an increasing adoption of cancer-causing behaviors, particularly smoking, in developing countries (Jemal et al., 2011).

Among of all cancers, malignancies of Gastrointestinal (GI) tract are the most important ones in terms of their broad spectrum and overall incidence. GI cancers account for 20% of estimated new cancer cases and 15% of estimated death worldwide (Herszenyi and Tulassay, 2010). American Cancer Society reported, each year, GI cancers diagnosed in more than 275,000 people and nearly 136,000 die because of these diseases (2009). According

to the latest Global Report on Cancers, esophageal, gastric and colorectal cancers are respectively ranked as the eighth, fourth and third most common type of cancer worldwide, as well as common causes of cancer related death in the world (Herszényi and Tulassay, 2010). It seems with rapid economic development and the westernization of lifestyle, many developing nations have experienced increasing incidence rates in gastrointestinal malignancies. While the Middle East, including Iran, is considered as a low risk region for colorectal cancer, but gastric and Esophageal Cancer are still common dangers in some parts, especially in the north provinces of Iran (Hosseini and Izadpanah, 2004; Najafi et al., 2011). Each year, approximates 50,000 new cases of cancer occur in the 75 million Iranian population. The most common organ system involved with more than 38% of all cancers is the GI track (Pourhoseingholi, 2008). However there are few data about incidence trends in this region.

Monitoring cancer incidence and time trends is essential for cancer research and health care planning. Cancer incidence is known to vary from region to region. The study of the epidemiology and the pattern of cancer may throw some light on the etiology of the disease. A systematic trend analysis may help to understand the

<sup>1</sup>Department of Biostatistics, Faculty of Medical Sciences, <sup>2</sup>Department of Biostatistics, Tarbiat Modares University, <sup>4</sup>Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, <sup>3</sup>Gastrointestinal and Liver Diseases Research Center. Guilan University of Medical Sciences, Rasht, Iran \*For correspondence: [kazem\\_an@modares.ac.ir](mailto:kazem_an@modares.ac.ir), [ghanai@yahoo.com](mailto:ghanai@yahoo.com), [ghanai@gums.ac.ir](mailto:ghanai@gums.ac.ir)

alterations in incidence with regard to time, place and person distribution and changing cancer risk. These trends will indicate the increasing burden of cancer if any, and help in making future projections on the load of cancer and requirements for management. However, there have been a variety of studies about epidemiologic pattern, incidence trends and etiology of GI malignancies in some provinces of Iran for instance, Golestan and Kermanshah, a few number of similar studies have been conducted in Guilan province. In this population-based cancer study, it has been tried to assess the epidemiologic trend of GI cancers in Guilan province over a 15 years period from 1997 to 2011.

## Materials and Methods

### Study setting

Guilan is one of the northern provinces of Iran. It is about 235 kilometers long and between 25-105 kilometers wide. It lies along the Caspian Sea, just west of the Mazandaran province, east of the Ardabil province, north of the Zanjan and Qazvin province. It is more than 14000 square kilometer and has a population about 2.5 million (49.8% male, 50.2% female).

### Data source

In this longitudinal study, the registered data for all patients diagnosed with gastric, esophageal and Colorectal Cancers in Guilan province during the 15 years period were included.

The Guilan Cancer Registry System conducted by the Gastrointestinal and Liver Diseases Research Center (GLDRC) of Guilan University of Medical Sciences and Guilan Provincial Health Center data were used to identify new GI tract cancer cases during the study period. Regarding cancer forms, we have selected the most widespread GI malignant tumors in this region, namely Esophageal Cancer (EC), gastric cancer and Colorectal Cancer (CRC). The International Classification of Diseases, 10<sup>th</sup> revision (ICD-10), was used for cancer classification. According to this classification esophageal, gastric, colon and rectal cancers were defined by C15, C16 and C19-C21 codes respectively. After data collection, all data were alphabetically arranged and duplicate cases with the same name, sex, age and place of residence were removed.

According to the address, the referred cases from neighboring provinces were excluded. The population of Guilan in 1996 and 2006 was extracted from Statistical Center of Iran and the population for the years 1997-2005 and 2007-2010, which were unavailable from the Statistical Center of Iran database, were estimated using the expected population growth rate during these years (with 0.7% population growth per year). The population was divided into eight age groups (0-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, ≥75 years).

### Statistical methods

Age specific incidence rates were calculated for each cancer in each year by dividing the number of cancers diagnosed by the population of Guilan at the same year

and reported as the number per 10<sup>5</sup> persons per year (person-year). Also Age-standardized incidence rates (ASR) were calculated by the direct method, using the world standard population (Suárez et al., 2009). The Fay and Feuer method was used to calculate the 95% confidence interval for standardized incidence rates. Data were entered into the word excel spreadsheet, and the Statistical Package for Social Sciences (SPSS18.0) was used for statistical comparison. For analysis of trend incident rates, the Cochran-Armitage test in Winpepi 2.1 software was used. Also Long-term trends in age-standardized cancer incidence rates were analyzed using Joinpoint regression (segmented regression), which fitted up to two joined straight lines on algorithmic scale to the trends in the annual rates. The trends of various periods were described by the annual percent change (APC). The average annual percent change (AAPC) was estimated as a geometric weighted average of the APCs in the period of 1997 to 2011 weighed by the length of internals. The Joinpoint analyses were performed using the 'Joinpoint' 4.0.1 software. A p value of less than 0.05 was considered statistically significant.

## Results

During, the study periods 8332 cases of GI cancer were founded and registered in Guilan province. These included 5259 men (63.1%) and 3073 (36.9%) women, as shown in table 1. The mean age at diagnosis for esophageal, gastric, colon and rectal cancers were 63.9±11.4, 63.3±12.5, 56.1±16.9 and 58.4±14.5 years, respectively. Annual crude rates in addition to age-specific and standardized incidence rates of GI cancers are shown in Tables 1 and 2.

### Esophageal cancer

In EC, the standardized incidence rate (ASR) during the 15 years period showed fluctuations. The incidence was higher in men, but overall, there was a decreasing trend from 6.26 [95%CI:(4.14-8.38)] in 1997 to 4.36 [95%CI:(3.52-5.2)] in 2011 (Table 2 and Figure 1). Cochran-Armitage test for incidence trend showed statistically significant differences in incidence of EC over 15 years period of study (p<0.001). The ASR for EC was 5.97 in this period. Changing trends in ASRs in Joinpoint analysis showed declining by 3% per year [(95%CI:-4.8-(-1.2)] from 1997 to 2011 (Table 4).

### Gastric cancer

During the study period, ASRs for gastric cancer showed a steady stabilized pattern (Figure 1). Although the ASR was higher in the end of the study period (14.89 in 1997 vs 15.38 in 2011), the Cochran-Armitage test for incidence trend showed no statistically significant

**Table 1. Distribution of GI Malignancies by Gender in Guilan Province from 1997 to 2011**

Sex	Esophagus N (%)	Gastric N (%)	Colon N (%)	Rectum N (%)	Total N (%)
Female	647 (7.8)	1195 (14.3)	812 (9.7)	419 (5.0)	3073 (36.9)
Male	957(11.5)	2900 (34.8)	892(10.7)	510 (6.1)	5259 (63.1)
Total	1604(19.3)	4095 (49.1)	1704(20.5)	929(11.1)	8332(100.0)

**Table 2. Crude Rates (CR), Age-Specific and Standardized Rate (10<sup>5</sup>) (ASR) by Calendar Year for Gastric and Esophagus Cancer in Guilan Province**

TYPE	AGE GROUP	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	
Gastric	0-14	0.12	0	0	0	0	0	0	0	0.19	0	0	0	0	0	0.19	
	15-24	0.22	0.22	0.89	0	0.44	0	0.37	0.18	0.75	0.18	0.37	0.18	0.18	0.18	0.18	
	25-34	1.75	2.62	2.33	3.79	1.45	1.16	1.69	1.93	1.45	1.69	1.21	0.96	1.69	0.72	0.48	
	35-44	4.6	8.43	3.06	5.36	3.83	4.6	3.05	3.05	3.61	3.61	5.28	4.17	5	5.28	3.89	
	45-54	22.8	15.83	18.37	15.2	17.1	15.2	7.26	8.79	13	8.41	14.14	13.38	17.97	17.97	16.44	
	55-64	11.2	8.96	11.2	20.16	11.2	14.18	11.73	9.78	16.3	16.3	9.12	17.6	44.99	38.47	43.68	
	65-74	95.06	110.23	93.03	101.12	79.89	105.17	75.82	67	95.21	95.21	20.27	73.17	96.97	93.45	94.33	
	75+	116.8	106.18	116.8	134.5	120.34	134.5	72.51	93.46	93.46	25.78	116.03	65.8	116.03	154.7	175.65	
	CSR	11.46	11.28	10.38	11.59	10.21	10.3	12.06	9.85	11.72	11.72	4.4	20.6	12.72	13.88	14.42	
	ASR	14.89	14.2	13.98	14.84	13.32	13.26	12.21	11.91	11.99	11.99	11.65	10.59	12.91	13.69	14.24	
	CI	(13.74-16.04)	(13.22-15.18)	(12.82-15.18)	(13.63-16.05)	(12.07-14.57)	(12.18-14.34)	(10.58-13.84)	(10.71-13.11)	(10.89-13.09)	(10.51-12.79)	(9.39-11.79)	(11.79-14.03)	(12.2-15.18)	(12.2-15.18)	(12.74-15.74)	(13.8-16.96)
	0-14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	15-24	0.22	0.22	0.87	0	0.29	0	0.48	0	0	0	0	0	0	0	0	
	25-34	0	0.29	0.87	1.16	0.86	0.86	2.68	1.66	2.78	2.78	1.66	0.55	1.94	0.83	0	
35-44	1.15	0.38	1.91	4.6	2.68	4.2	6.96	4.52	5.35	4.97	4.97	4.2	8.02	4.2	7.64		
45-54	8.86	10.77	9.5	8.86	53.76	31.29	36.58	39.12	37.81	41.07	41.07	32.6	20.86	20.21	18.25		
55-64	55.25	42.56	51.52	53.01	42.46	50.56	31.73	38.79	37.81	29.97	37.81	23.8	35.26	35.26	26.44		
65-74	46.51	42.47	38.42	46.51	53.09	56.63	19.3	38.67	22.56	35.45	37.06	51.56	51.56	61.23	56.4		
75+	49.55	46.01	49.55	46.01	4.32	5.08	4.28	4.57	3.7	4.4	3.7	5.57	5.57	5.11	4.84		
CSR	6.26	6.15	6.16	7.03	5.62	6.54	4.39	3.76	4.67	4.67	3.59	3.59	5.65	5.17	4.93		
ASR	(4.14-8.38)	(4.06-8.24)	(4.1-8.22)	(4.58-9.21)	(3.63-7.61)	(4.47-8.61)	(3.19-5.59)	(3.76-5.62)	(30.1-6.33)	(2.64-6.32)	(1.8-5.38)	(5.12-6.18)	(6.25-6.09)	(4.03-5.83)	(4.03-5.83)		
CI	(4.14-8.38)	(4.06-8.24)	(4.1-8.22)	(4.58-9.21)	(3.63-7.61)	(4.47-8.61)	(3.19-5.59)	(3.76-5.62)	(30.1-6.33)	(2.64-6.32)	(1.8-5.38)	(5.12-6.18)	(6.25-6.09)	(4.03-5.83)	(4.03-5.83)		

**Table 3. Crude Rates (CR), Age-Specific and Standardized Rate (10<sup>5</sup>) (ASR) by Calendar Year for Colon and Rectum Cancer in Guilan Province**

TYPE	AGE GROUP	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
COLON	0-14	0.64	0.25	0.38	0	0.77	0.12	0	0	0.19	0.19	0.78	0	0	0.19	0
	15-24	0.67	0.22	0.67	1.12	0.89	0.67	0	0.18	0.75	0.56	0.75	0.75	0.37	0	0.18
	25-34	1.16	1.45	1.16	2.33	0.29	1.45	1.45	0.48	1.45	0.96	1.45	0.72	1.45	1.45	0.96
	35-44	4.98	2.68	3.83	3.45	2.68	3.06	2.22	4.72	3.61	2.78	2.78	5.56	4.17	7.28	5
	45-54	6.96	7.6	5.7	7.6	7.6	7.6	8.41	8.02	7.64	8.41	7.26	16.05	14.14	15.29	12.61
	55-64	5.22	5.97	7.46	7.64	6.72	3.73	3.26	5.86	11.08	11.08	9.12	8.47	26.73	33.25	33.25
	65-74	24.27	18.2	23.25	19.21	29.32	20.22	14.98	21.15	27.33	20.27	21.15	22.04	20.27	39.67	35.26
	75+	7.08	17.6	28.31	21.23	38.93	7.07	8.05	24.17	20.95	25.78	32.23	53.18	53.18	58.01	48.34
	CSR	3.43	2.7	3.34	3.83	3.79	3.12	3.16	3.79	4.69	4.4	4.74	7.4	4.7	8.35	7.4
	ASR	4.09	3.46	4.11	4.77	4.73	3.85	3.25	4.76	3.87	4.49	4.82	4.63	4.63	8.27	8.41
	CI	(3.37-4.81)	(2.57-4.3)	(3.35-4.99)	(3.91-5.63)	(3.85-5.61)	(3.03-5.7)	(2.31-4.19)	(4.02-5.5)	(2.15-5.59)	(3.63-5.35)	(4.02-5.62)	(3.777-5.49)	(7.11-9.43)	(7.23-9.59)	(6.43-8.67)
	0-14	0	0.12	0	0.12	0	0	0	0	0	0	0	0	0	0	0
	15-24	0.22	0.22	0.22	0.44	0.22	0.22	0	0.24	0.48	0.72	0.72	0	0.18	0.37	0.18
	25-34	0.29	1.16	0.58	0.89	0.58	0.58	0.58	0.48	0.48	0.24	0.72	0.72	0.48	0.48	0.96
35-44	1.53	2.3	1.15	1.53	2.68	1.53	1.39	4.17	3.82	4.97	2.5	1.39	2.22	3.05	3.33	
45-54	1.9	5.7	4.43	5.7	4.43	5.7	2.29	4.58	4.58	4.58	4.97	4.2	4.58	8.41	8.02	
55-64	8.21	0.74	1.49	1.49	0.74	0	0	0.65	0	0	0	17.6	17.6	14.99	22.16	
65-74	5.05	12.13	11.12	11.12	14.15	13.14	5.28	22.04	12.34	15.86	15.86	11.46	11.46	18.51	20.27	
75+	7.07	14.15	3.53	14.15	17.69	14.15	6.44	9.66	8.05	16.11	16.11	20.95	22.56	35.45	41.9	
CSR	1.02	2	1.56	1.87	2	1.65	2.12	2.16	2.78	2.78	2.4	2.4	3.41	4.49	4.07	
ASR	1.28	2.51	1.97	2.41	2.53	2.13	2.11	2.31	2.75	2.79	2.4	2.4	2.5	4.43	4.17	
CI	(0.44-2.21)	(2.10-2.92)	(1.64-2.3)	(2-2.82)	(2.12-2.096)	(1.8-2.46)	(1.56-2.66)	(1.98-2.64)	(2.46-3.04)	(2.5-3.08)	(2.03-2.77)	(1.86-3.14)	(3.59-5.27)	(3.36-5)	(4.51-6.39)	

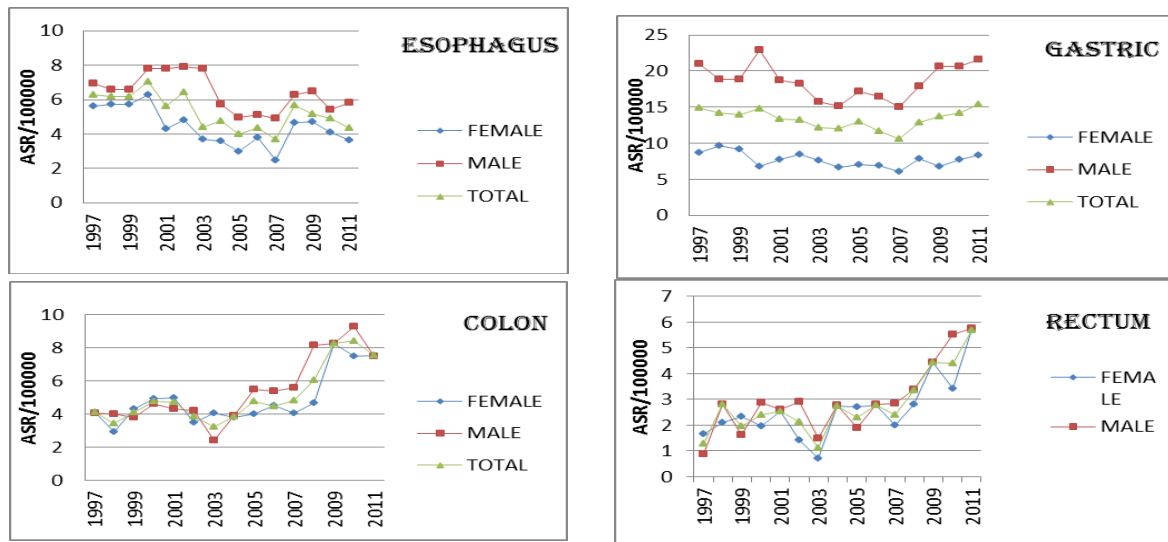


Figure 1. Trends for ASRs (per 100,000) by Sex During 1997-2011 in Guilan Province, Using the World Standard Population

Table 4. ASR and Joinpoint Analysis for GI Cancers from 1997 to 2011 in Guilan Province

Site	Period	Trend1		Trend2			
		APC	CI (%95)	APC	CI (%95)		
Gastric	Male	1997-2003	-5.2*	(-9.4-(-0.88))	2003-2011	4.2*	(1.2-7.3)
	Female	1997-2000	-12.1*	(-2.8-0.2)		0.7	(-1.1-2.5)
	Total	1997-2003	-5.8*	(-8.2-(-3.4))		1.7*	(1.0-4.4)
Esophagus	Male	1997-2011	-1.1	(-3.1-1)			
	Female	1997-2011	-4.2*	(-6.6-(-1.8))			
	Total	1997-2011	-3	(-4.8-(-1.2))			
Colon	Male	1997-2011	6.4*	(3.5-9.3)			
	Female	1997-2011	5.3*	(2.6-8)			
	Total	1997-2003	-0.9	(-7.2-5.8)	2003-2011	9.9*	(5.4-14.7)
Rectum	Male	1997-2011	8.2*	(4.3-12.2)			
	Female	1997-2011	6.9*	(2.1-11.9)			
	Total	1997-2011	7.3*	(4-10.6)			

\*The annual percent change is significantly different from 0 (two-side p<0.05); APC: annual percent change

differences in incidence of gastric cancer over 15 years period of study (p<0.001). Changing trends in ASRs in Joinpoint analysis showed declining by 5.8% per year [(95%CI: -8.2-(-3.4))] from 1997 to 2003 and increasing by 2.7% per year (95%CI: 1-4.4) from 2003 to 2011. In men, ASR showed declining trend by 5.2% per year [95%CI: (-9.4)-(-0.88)] from 1997 to 2003 and then rose by 4.2% (95%CI: 1.2-7.3) per year up to 2011. In women, ASRs showed statistically significant declining trend by 12.1% per year [95%CI: (-23-0.2)] from 1997 to 2000 and then increased up to 2011, but this increasing was not statistically significant in Joinpoint analysis (Table 4). It seems the incidence of gastric cancer raised with age so that the age group ≥65 showed higher incidence than those in other age group. Like EC ASRs for gastric cancer was higher in men compared to women.

Colon cancer

The results indicated that the incidence of colon cancer raised during the 15 years period. In 1997, the ASR for colon cancer calculated 4.09 while it increased up to 7.55 in 2011 (Table 3). Cochran-Armitage test showed significant difference in incidence of colon cancer over this period (p<0.001). In total, ASRs for colon cancer in

Guilan showed increasing pattern; leveling off from 1997 to 2003 and increasing by 9.9% per year from 2003 to 2011 (Table 4). The average annual percent change calculated 9.2% and 12.2% in the last five and ten years, respectively.

Rectal cancer

Similar to colon cancer, the incidence of rectal cancer increased during the study period. The ASR for rectal cancer was 1.42 in 1997 while it was 5.7 in 2011 (Table 2). This was a significant increase in Cochran-Armitage test (p<0.001).

The results of Joinpoint analysis on ASRs showed statistically significant raises for both sexes so that overall, the estimated annual percentage change was 6.4 in men and 5.3 in women over the 15 year’s period (Table 3).

Discussion

EC is the eighth most common cancer in the world and ranks sixth among all cancers related mortality (Fang et al., 2012). There is an obvious difference in EC incidence between men and women. For men, the incidence is times higher than that for women (Zhang et

al., 2012). EC incidence and mortality are also affected by geography. Eastern Asia and eastern and southern Africa have the highest rates, though, Europe and North America show lower rates. In males, the highest incidence of EC is observed in southern Africa (ASR 22.3 per 10<sup>5</sup>), eastern Asia (ASR 20.3 per 10<sup>5</sup>), and eastern Africa (ASR 14.9 per 10<sup>5</sup>). Similarly, these areas are also sites of the highest incidence among females, however the greatest burden of EC occurs in the “Asian EC Belt”, extending from northern Iran, to east China, and north of Russia (Glenn, 2001).

International Agency for Research on Cancer and Institute of Public Health Research (IARC-IPHR)(1968-1971), cancer Registry documented the high rates of EC in some parts of northern Iran for the first time (Mohagheghi and Mosavi, 2010). This 3-year cancer registry showed 10 and 30 fold variation in EC incidence rates among women and men, respectively, in this geographic area. In Rasht city, located in the southwestern Caspian littoral, and its surrounding areas, age standardized incidence rate were as low as 10-20/10<sup>5</sup> for men and 3-10/10<sup>5</sup> for women. Low rates and a male-dominant incidence pattern were similar to epidemiologic patterns of EC in most of the western world. In contrast, in the southeastern part of this littoral, in areas surrounding Gonbad city and further to the East, rates were at least as high in women as in men, and were some of the highest rates for any single Cancer ever reported anywhere in the world (ASR>100/10<sup>5</sup>) (Mahboubi et al., 1973).

The result of present study showed the incidence of EC has a declining trend in Guilan province during the 15 years of study period. The incidence was higher in men compared to women. These results are consistent with data from other regions of the world. Comparing these results with data from other neighboring provinces represent a lower incidence of EC in Guilan Province. A study conducted in Ardebil (1996-1999) showed ASR for EC was 15.4 and 14.4 for men and women respectively (Sadjadi et al., 2003). Another study in East Azerbaijan province reported higher incidence of EC compared to Guilan province in the same period. According to this study ASR for EC in 2006-2007 was 12.43 in men and 11.65 in women (Somi et al., 2008). Mohebbi et al. (2008) reported ASR of 14.61 and 12.73 in Mazandaran province from 2001 to 2005 in men and women, respectively.

Some studies in Turkmen plain suggest a declining incidence of EC in this region, compared to those reported 30 years ago. In fact, ASR of 165.5 per 10<sup>5</sup> in males and 195.3 per 100 thousand in the 1970's had reduced to 43.4 and 36.3 per 10<sup>5</sup> respectively for males and females (Semnani et al., 2006; Mohbbi et al., 2008). In Iran, several studies have examined the incidence of EC. According to a study carried out in Kerman (1996-2000), ASR was 3/10<sup>5</sup> and 1.8/10<sup>5</sup> for men and women, respectively (Sadjadi et al., 2007). Another study in Fars province reported ASR of 1.05 for EC (Mehrabani et al., 2008). A study conducted in Kermanshah province showed decreasing trend in the incidence of EC from 1993 to 2007. The incidence decreased from 10.7/10<sup>5</sup> (95%CI: 8.3-13.9) in 1993 to 5.0/10<sup>5</sup> (95%CI: 3.8-6.5) in 2007. The drop in the annual incidence of this cancer in Kermanshah Province was 0.36

per 10<sup>5</sup> [95%CI:-0.70-(-0.02)]. The ASR of EC was 8.1 per 10<sup>5</sup> over 15 years (Najafi et al., 2011).

Gastric cancer is the fourth most commonly diagnosed cancer and the second leading cause of cancer death worldwide (Jemal, 2010). In accordance with most of the common forms of cancer, there is considerable geographic variation in incidence of gastric cancer around the world. High-risk areas (ASR in men >20 per 10<sup>5</sup>) include East Asia, Eastern Europe, and parts of Central and South America (Brenner et al., 2009). The intermediate risk areas are those populations with an ASR between 10 and 20 and low risk populations are those with an ASR of less than 10 like the USA and Canada (Malekzadeh et al., 2009). Steady and persisting falls in rates were observed in European countries, and the fall between 1980 and 1999 was 50% in the European Union (EU), 45% in Eastern Europe and 40% in Russia. However, the declines were greater in Russia and Eastern Europe, since rates were much higher, in absolute terms. Joinpoint regression analysis indicated that the falls were proportionally greater in the last decade for men (3.83% per year in the EU) and in the last 25 years for women (3.67% per year in the EU) than in previous calendar years (Levi et al., 2004).

Gastric cancer stands as the most common and accounting for 50% of all GI cancers in Iran (Haghdost et al., 2008). The incidence of the gastric cancer is also very high compared with western countries. There is an obvious variability in the incidence rates of gastric cancers within Iran. As the ASR for gastric cancer in males is less than 10 in southern Iran, it gradually increases as we move from south to north of the country. It approaches 50 in northwestern Iran (49.1 for men and 25.4 for women in Ardabil) (Sadjadi et al., 2003; 2005; Malekzadeh et al., 2004). In Semnan (Babaei et al., 2005), East Azerbaijan (Somi et al., 2008), Mazandaran-Golestan (Mohebbi et al., 2008) and Kerman (Sadjadi et al., 2007), ASR reported 36.9, 25.99, 26.78, 10.2 for men and 14.8, 11.60, 11.25 and 5.1 for women.

The result of a study in Western Iran revealed, the incidence of gastric cancer raised with age so that the age group ≥80 showed 3.2 times higher incidence than those in age group 60-69 years. The standardized incidence during the 15 years period showed great fluctuations but overall, there was a decreasing trend from 10.6/10<sup>5</sup> (95%CI: 8.2-13.9) in 1993 to 9.1/10<sup>5</sup> (95%CI: 7.4-11.1) in 2007 (Najafi et al., 2011). A cross-sectional population-based study from 2000 to 2005 designed by Handrail et al. (2012) the ASR in Iran was significantly increased from 2.8 in 2000 to 9.1 per 10<sup>5</sup> persons per year in 2005. In men it increased from 4.1 in 2000 to 13.1 per 10<sup>5</sup> persons and in women from 1.5 in 2000 to 5.0 (Haidari et al., 2012).

The present study revealed that despite high incidence of gastric cancer in Iran especially in neighboring provinces of Guilan, rank as the intermediate risk areas for gastric cancer and has stabilized trend during 15 years previous. The evidence indicates that one of the leading causes of gastric cancer is *Helicobacter pylori*. It seems the main reasons for the steady stabilized trend of gastric cancer in Guilan is in line with early diagnosis, treatment and eradication of *H pylori* infection in this region during last decades. Gender is an important factor in all studies

of medical sciences, mainly cancer studies. As it was observed, gastric cancer incidence in our study was much higher in men than in women. Some researchers have attributed the cause of such difference to the protective role of female hormones (Chandanos and Lagergren, 2008). In addition, the sensitivity of individual health care in women is much higher than in men and this may lead to better and earlier diagnosis of precancerous state among women.

Cancers of the Colon and rectum are rare in developing countries, while it occurs in high incidence rates in countries of Europe, North America, Australia and Japan (Feraý et al., 2008; Khuhaprema and Srivatanakul, 2008). The rising incidence of CRC in Asian countries during the last two decades has recently been reported by an Asia Pacific Consensus (Sung et al., 2008). ASR of CRC in more developed regions of the world estimated for the year 2008 has been reported to be 37.7 and 24.3 per 10<sup>5</sup> males and females, respectively (Feraý et al., 2008). In the South East Asian Region, the ASR was 5.6 and 7.4 in males and females respectively (Feraý et al., 2008). Increasing incidence of CC in Hong Kong was mostly in the older and male population, but not in the younger age group (Yee et al., 2010). In Asia, CRC incidence increased from 1983-87 to 1998-2002 for both males and females, except in Mumbai (Center et al., 2009).

According to a recently published pathology-based national Iranian cancer registry, the ASR for CRC in males has increased from 5.5 to 8.2; however, Iran is still a low-risk country for CRC, particularly in the older population. Although the ASR in the young Iranian and the US population is close, the rates are much lower in older Iranians (Mousavi et al., 2009). In the west of Iran, the male to female ratio was 1.2:1. The age standardized incidence rate was significantly increased from 1.5 cases per 10<sup>5</sup> per year in 2000 to 4.8 cases in 2005 (Abdifard et al., 2013). According to Safaee et al (2012) report, the male to female sex ratio was 1.3:1. Also overall ASR in the four years period was estimated 38.0 per 10<sup>5</sup> and 39.96 and 36.16 per 10<sup>5</sup> in male and female respectively, that is considered as relatively high rate compared to other Asian countries.

Although CRC raised in recent years, the remarkable point is that most of these studies have reported the incidence of CRC lower than the global average so the incidence of CRC in Fars (Mehrabani et al., 2008), Ardabil (Sadjadi et al., 2003), Semnan (Babaei et al., 2005), East Azerbaijan (Somi et al., 2008), and Golestan-Mazandaran (Mohebbi et al., 2008) was 3.26, 7.9, 11.42, 7.55, 15.6 in men and 2.41, 5.9, 10.52, 6.86, 9.73 in women.

In Guilan province, upward trend in the incidence of CRC was seen from 1997 to 2011. Although this upward trend is statistically significant, comparing the results with neighboring provinces and other regions of the world shows CRC incidence is still low in Guilan province. Like other regions, the incidence is higher in men and the incidence rate raises with age. It seems this increase in incidence trend can be attributed to improved diagnostic and screening methods, early identification of patients and increased prevalence of risk factors such as western dietary patterns, obesity and low physical activity. Also

the etiology of CRC may be different in Guilan and should not forget the role of genetic factors.

In the interpretation of findings of this study, some limitations should be kept in mind. First, our analyses are based on data on GI cancer incidence by age, sex, anatomic site and morphologic type. Some additional factors helpful in determination of screening strategies, such as stage of disease, were not available. Another limitation of our study results from the retrospective nature of the survey from 1997 to 2003. As a result of poor quality of keeping medical records in medical centers especially in private ones, the incidence of GI cancer maybe has been underestimated in this period. In addition, we did not have access to details of the information such as anatomic and pathologic subtype of tumor. For this reason, we could not use a better categorization for comparison of these subtypes incidence trend in our study. Especially in EC, this limitation was prominent while most study reported decreasing trend for Squamous cell carcinoma and reverse trend for adenocarcinoma in recent decades.

In conclusion, in all gastrointestinal malignance is in Guilan, male domination was observed. While EC revealed a decreasing trend in incidence, gastric cancer showed steady stabilized pattern and the trend for colon and rectal cancer raised over last 15 years. Cancer is the result of concurrent effect of environmental factors and genetic susceptibility, and the way of living and behaving is one of the most important influencing factors. Considerable effort has to be made to increase the public awareness and interests on health issues.

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