



## Temporal and geographical variations in colorectal cancer incidence in Northern Iran 2004–2013



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### ABSTRACT

**Introduction:** Colorectal cancer (CRC) is one of the most common cancers in the Golestan province, Northern Iran. The purpose of this study is to describe colorectal cancer incidence patterns and trends in the province 2004–2013.

**Methods:** Data on CRC cases were obtained from the Golestan Population-based Cancer Registry (GPCR). The GPCR is a high-quality cancer registry that collects data on primary cancers according to internationally accepted standard protocols. Age-standardized Incidence rates (ASR) were calculated and the 10-year trend quantified using the average annual percentage change (AAPC) from Joinpoint regressions.

**Results:** The overall ASR of CRC were higher in men (14.8 per 100,000 person-years) and the urban populations (35.4), relative to women (11.5) and the rural populations (17.1), respectively. The overall incidence rate was observed to significantly increase 2004–2013 in men (AAPC = 7.3; 95%CI: 2.9–11.8) and women (AAPC = 6.6; 95%CI: 2.7–10.6). The analysis also showed that urban areas (AAPC = 8.1; 95%CI: 2.4–14.1) had a relatively more rapid increase in rates compared to rural areas (AAPC = 6.9; 95%CI: 2.2–11.7).

**Conclusions:** CRC incidence rates in Golestan have been rising during the most recent decade, with a higher incidence and more rapid increases among men and the urban populations. The underlying risk factors should be assessed in the context of developing CRC prevention interventions in Golestan.

### 1. Introduction

With over 1.2 million new cases worldwide, colorectal cancer (CRC) has emerged as a major public health problem, ranking as the third most common cancer in men and second in women. [1–3] Estimates indicate that the worldwide burden of CRC incidence will increase by 60% with more than 2.2 million new cases expected by 2030 [4]. More

than half of the cases (55%) occur in developed countries [1]. There are wide geographical variations in CRC incidence rates across the world, with men being more affected than women [5,6]. Incidence rates differs ten-fold globally, both in men and women.

There are different risk factors associated with the incidence of CRC. Age and hereditary or genetic predisposition are not-modifiable factors. Environmental exposures and lifestyle, which are potentially

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modifiable, may play a crucial role to increase the likelihood of development of colorectal cancer. [6] Alcohol intake, low physical activity, obesity, higher intake of red and processed meat has been reported to increase CRC risk, while intakes of dietary fiber, green leafy vegetables, some micronutrients such as foliate, and calcium were considered as protective factors [7].

In Golestan province, in North of Iran, CRC is the fourth most common cancer in men and the fifth most common cancer in women. [8] The growing trends in colorectal cancer incidence is of concern, and it should be considered as a priority in health policy making in this region [7].

In this paper we describe the changing patterns and trend in CRC over the last decade in Golestan using incidence data from the Golestan Population-based Cancer Registry (GPCR). This data is considered of high quality [9,10], having been included in *Cancer Incidence in Five Continents*, the series edited by the International Agency for Research on Cancer (IARC) that provides a compilation of such datasets worldwide.

## 2. Methods

Golestan province is located in Northern Iran. Total population of Golestan province in 2013 was 1,845,330 (about 2.3% of total population of Iran) of which 926,934 (50.2%) were men. The land area of Golestan province is about 1.3% of total land area of Iran. Table 1 shows the distribution of Golestan population by age groups and gender. About 50% of Golestan populations lived in urban areas (cities).

This study was conducted based on data from the GPCR, which registers all primary cancer cases by considering the methods, guidelines, standards and definitions of the International Agency for Research on Cancer (IARC) and International Association of Cancer Registries (IACR). [9,11] The methods of data collection in GPCR have been described previously [10,12]. Briefly, the GPCR collects data on primary incident cases of cancers from all public and private diagnostic and therapeutic centers (hospitals, pathology/laboratory centers, imaging centers and selected specialist physician's offices), including and primary health centers, throughout the Golestan province. Data is collected by using passive and active methods. Data on cancer mortality are obtained from the Golestan death registry unit. The Third edition of the International Classification of Disease for Oncology (ICD-O-3) was used for coding tumor characteristics [13]. Collected data were entered into the software CanReg-5, an open source and free software published by IARC. [14] For quality control of the data, different indices were

**Table 1**  
Distribution of Golestan population by age groups and gender, 2013.

Age group	Male		Female	
	Number	Percent	Number	Percent
0-4	87743	9.47	84294	9.18
5-9	75968	8.20	73171	7.97
10-14	68273	7.37	65693	7.15
15-19	78384	8.46	77077	8.39
20-24	107624	11.61	105615	11.50
25-29	108645	11.72	111269	12.12
30-34	91411	9.86	92392	10.06
35-39	72896	7.86	71371	7.77
40-44	57411	6.19	57917	6.31
45-49	46949	5.06	46119	5.02
50-54	40251	4.34	39618	4.31
55-59	29183	3.15	29920	3.26
60-64	19326	2.08	21988	2.39
65-69	14338	1.55	15573	1.70
70-74	9748	1.05	9927	1.08
75-79	9530	1.03	8200	0.89
80-84	5628	0.61	5010	0.55
> 85	3626	0.39	3242	0.35
Total	926,934	100.00	918396	100.00

used such as the proportion of cases with microscopic verification (MV %), cases diagnosed only by death certificate (DCO%), cases with unknown age, and cases with unknown primary site.

For the present study, we obtained 10-year data on CRC cases from the GPCR (2004–2013). Number of cases, age-specific incidence rates, crude rates and age-standardized incidence rates (ASR) were calculated directly using the CanReg-5 software. [14] The World Standard Population was used for calculating the ASRs [15]. Population data were obtained from annual census of the statistics office of the Deputy of Health of the Golestan University of Medical Sciences (GOUMS). The rates were separately calculated by year and sex. We also calculated and presented incidence rates for urban (residents of cities) and rural population (residents of villages). Indices of data quality were calculated and reported for different years.

To examine incidence trends, we calculated the Average Annual Percent Change (AAPC) by sex and residence area using Joinpoint regression (version 4.6.0.0). The regression model was used to identify significant changes in the incidence rates from 2004 to 2013, with the trend in AAPC and corresponding 95% confidence intervals (CI) calculated. [16] The protocol of this study was approved by the Ethics committee of GOUMS.

## 3. Results

In total, 1615 new CRC cases were registered in the GPCR during the 10-year study period. More than half of patients (903, 56%) were men, and 1087 (67%) lived in urban areas, with the mean age of the CRC patients 56.6 (Standard Deviation, SD, 15.6) years. The results of quality assessment suggested acceptable ranges for the main indicators including MV% (78.35%) and DCO (3.9%).

The number of colorectal cancers, and the crude rate and ASR (per 100,000 person-years) are presented in Tables 2 and 3, respectively. The overall ASR was 14.8 in men and 11.5 in women, with rates twice as high (35.4) in urban compared with rural areas (17.1).

Joinpoint regression analysis indicates a statistically significant increasing trend on CRC incidence in the Golestan population, with the average increase per annum slightly higher in men (AAPC = 7.3; 95%CI: 2.9–11.8) than women (AAPC = 6.6; 95%CI: 2.7–10.6). Our data also suggested that statistically significant increasing trends in CRC incidence was observed in both urban (AAPC = 8.1; 95%CI: 2.4–14.1) and rural (AAPC = 6.9; 95%CI: 2.2–11.7) populations (Fig. 1).

According to ASR distribution of colorectal cancer through the Golestan province in Figs. 2 and 3, colorectal cancer highest rates were mostly located in western parts and urban areas. The highest incidence rates in western area was found for Gorgan, the capital city of Golestan province (ASR = 28.4 per 100,000 person-year).

## 4. Discussion

This paper provides a comprehensive overview of the incidence trends of CRC by using GPCR's data in Golestan province of Northern Iran in years 2004–2013. There was a significantly increasing trend in incidence of CRC among men and women in comparison with previous reports in this region. [10] This new finding is in line with the rising rates observed in many transitioning countries [1,4,17].

The economic growth in low-income and middle-income countries has changed, with adoption of an increasingly westernized lifestyle which may affect CRC risk, such as unhealthy diet (low consumption of fruits and vegetables, and high consumption of red/processed meats), obesity, smoking and physical inactivity. Moreover, the growth and aging of the population is leading to year-on-year increases in the number of colorectal cancer cases, irrespective of the changes in rates. [4,17–21]

Our result indicated that ASR of colorectal cancer in Golestan is higher in men (14.8) than in women (11.5), with the male excess not

**Table 2**

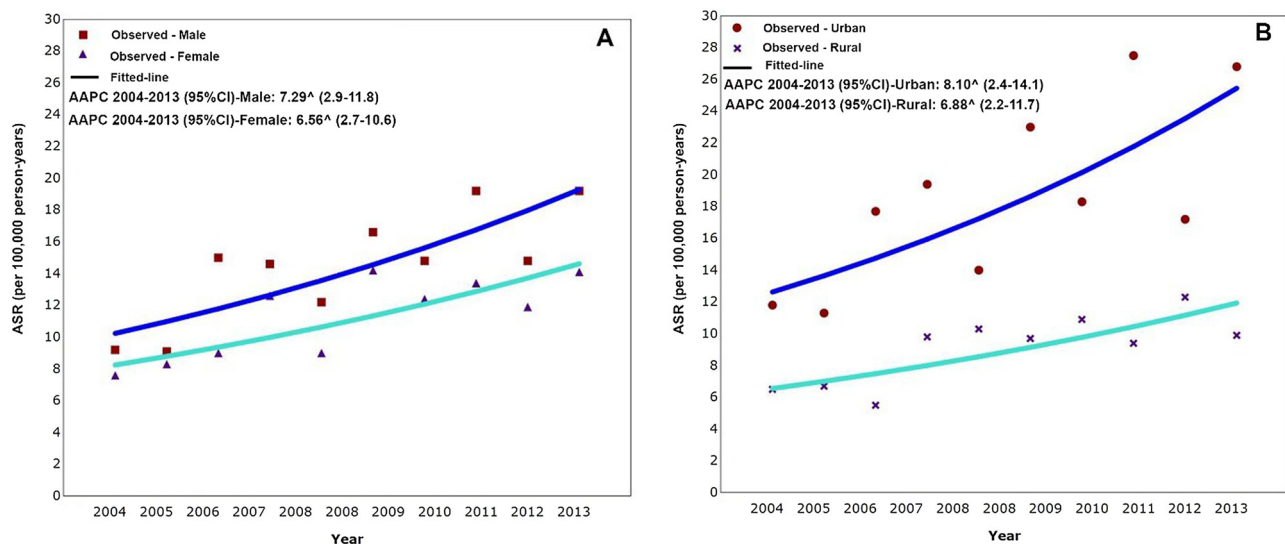
Number, crude rate, age standardized incidence rates (ASR) (per 100,000 person-year) of colorectal cancers in Golestan, Iran during 2004–2013 for men.

		Colon			Rectum			Colorectal		
		Number	Crude Rate	ASR	Number	Crude Rate	ASR	Number	Crude Rate	ASR
Residence Area	Total	650	15.12	21.3	253	5.88	7.9	903	21	29.2
	Urban	443	10.26	14.1	166	3.84	5.1	609	14.1	19.2
	Rural	207	4.86	7.2	87	2.04	2.8	294	6.9	10
Year	2004	33	4.11	5.7	19	2.36	3.5	52	6.47	9.2
	2005	38	4.67	7	14	1.72	2.1	52	6.39	9.1
	2006	57	6.89	10.8	21	2.54	4.2	78	9.43	15
	2007	68	8.08	11.8	20	2.38	2.8	88	10.46	14.6
	2008	53	6.21	8.7	22	2.58	3.5	75	8.79	12.2
	2009	73	8.51	11.9	30	3.5	4.7	103	12.01	16.6
	2010	60	6.91	10.1	32	3.69	4.7	92	10.6	14.8
	2011	93	10.44	14.1	32	3.59	5.1	125	14.03	19.2
	2012	71	7.84	9.9	39	4.31	4.9	110	12.15	14.8
	2013	104	11.22	15.4	24	2.59	3.8	128	13.81	19.2

**Table 3**

Number, crude rate, age standardized incidence rates (ASR) (per 100,000 person-years) of colorectal cancers in Golestan, Iran during 2004–2013 for women.

		Colon			Rectum			Colorectal		
		Number	Crude Rate	ASR	Number	Crude Rate	ASR	Number	Crude Rate	ASR
Residence Area	Total	526	12.47	17.5	186	4.41	5.8	712	16.88	23.3
	Urban	350	8.32	12	128	3.04	4.2	478	11.36	16.2
	Rural	176	4.15	5.5	58	1.37	1.6	234	5.52	7.1
Year	2004	29	3.67	5.8	12	1.52	1.8	41	5.19	7.6
	2005	30	3.75	5.8	13	1.62	2.5	43	5.37	8.3
	2006	41	5.04	7	13	1.6	2	54	6.64	9
	2007	57	6.89	10.2	15	1.81	2.4	72	8.7	12.6
	2008	48	5.71	7.6	10	1.19	1.4	58	6.9	9
	2009	60	7.1	9.8	27	3.2	4.4	87	10.3	14.2
	2010	57	6.66	9.6	19	2.22	2.8	76	8.88	12.4
	2011	68	7.76	9.9	25	2.85	3.5	93	10.61	13.4
	2012	61	6.83	8.8	23	2.58	3.1	84	9.41	11.9
	2013	75	8.17	10.3	29	3.16	3.8	104	11.33	14.1



**Fig. 1.** Jointpoint analysis of temporal variation in age-standardized incidence rates (ASR) colorectal cancer incidence in Golestan, by gender (A) and residence area (B).

<sup>^</sup>indicates that the Average Annual Percent Change (AAPC) is significantly different from zero at the alpha = 0.05 level.

dissimilar to that observed in many other areas of the world. The reasons for this variability are not completely understood, but partly it may be the result of different interactions between gender-specific genetic susceptibility to risk factors, as well as the protective influences of sex hormones. Gender-specific differences in screening practices may also

be explanatory, though there is little evidence to support these hypotheses at present. [1,22–24]

Our population-based analysis also demonstrated that CRC incidence rates were significantly higher in urban areas as compared to rural areas, probably linked to a differential in the prevalence and

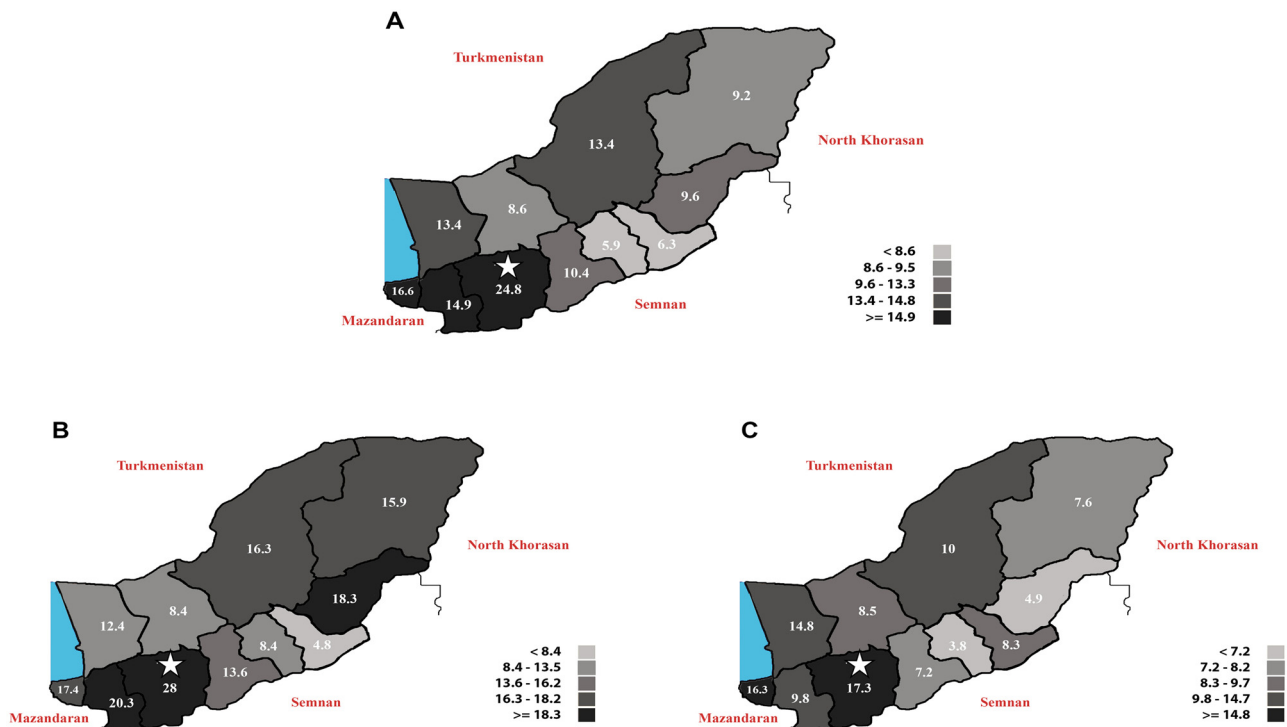


Fig. 2. Age-standardized incidence rates (ASR) (per 100,000 person-years) of colorectal cancer in Golestan, Iran (2004–2013)- Men. A = Total area; B = Urban area; C = Rural Area; ☆ Gorgan City (Capital of Golestan).

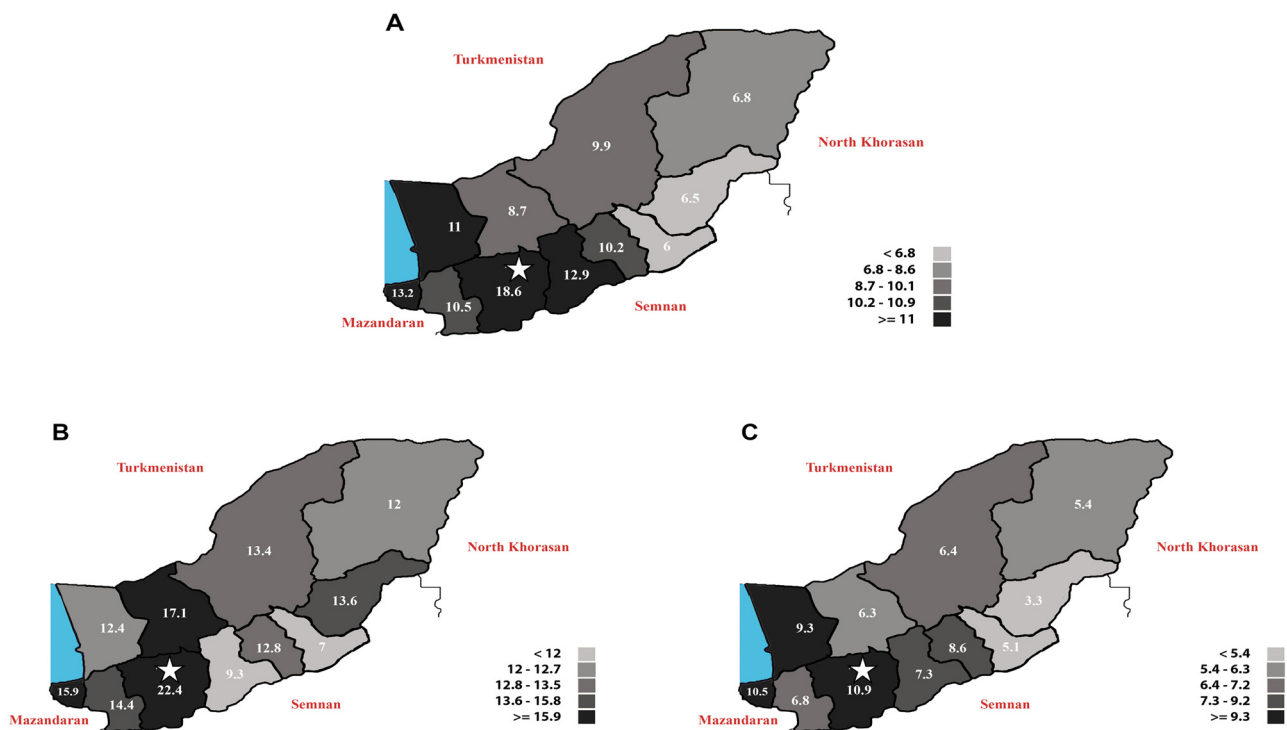


Fig. 3. Age-standardized incidence rates (ASR) (per 100,000 person-years) of colorectal cancer in Golestan, Iran (2004–2013)- Women. A = Total area; B = Urban area; C = Rural Area; ☆ Gorgan City (Capital of Golestan).

distribution of the above risk factors for CRC. [1,22] Other possible determinants are linked to barriers in terms of distance, and lack of access to primary care facilities, as well as financial barriers in rural areas, leading to lower levels of CRC diagnosis. [25–27]

Our findings also showed considerable geographic disparities in the incidence of CRC, with higher rates in Gorgan city (the capital of

Golestan province) and some of its neighboring cities, located in Western area of Golestan province. This part has been proposed to have relatively rapid development, urbanization and industrialization, and high concentration of medical services. There are different ethnic groups in the Golestan Province, the majority being Turkmen in the eastern part of the province, and Fars in western areas. However, we

did not have information on ethnicity in our database, and therefore could not perform specific analysis by ethnic groups. Different life-style patterns between ethnic groups and even different genetic interactions to the risk factors may explain the different CRC incidence in these regions. [28] Similar geographical disparities were reported from this region for the incidence rates of oesophageal cancer. Roshandel et al [10] described higher rates for esophageal cancer in Eastern parts of Golestan province as compared to Western parts. The disparities in CRC among different population subgroups identified by ethnicity and place of residence clearly need to be better understood in order that targeted interventions can be implemented.

## 5. Conclusion

This study suggests that there were increasing trends in CRC incidence in Golestan province during 2004–2013. Higher CRC incidence rates as well as more rapidly increasing trends were observed in men and the urban populations; we also observed higher rates in the western part of the province. In order to tackle the increasing risk of CRC in the province, the key local risk factors need to be identified, and effective and cost effective early-detection strategies prioritized by health policy makers.

## Authorship contribution

SuH: collaborated in data processing; collaborated in analysis; wrote the manuscript; AF, ShS, S-RK: initiated, conceptualized and designed the study; edited and critically reviewed manuscript; TA, S-MS, RH: collaborated in collection of data; critically reviewed manuscript; RA, MP, MN-T: interpreted results; critically reviewed manuscript; GR: conceptualized and designed the study; performed statistical analysis; wrote the manuscript; FB: edited and critically reviewed manuscript; collaborated in quality control; EW: edited and critically reviewed manuscript; collaborated in quality control; All authors read and approved the final manuscript.

## Conflict of interest statement

The authors declare no conflicts of interest for this article.

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