

# A Systematic Review Over the Incidence of Colorectal Cancer in Iran

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Received: November 30, 2014; Accepted: December 2, 2014

**Context:** Colorectal cancer (CRC) is the third most prevalent cancer worldwide which is less common in the Middle East. It is also the second leading cause of cancer-related mortality and represents a major public health problem in developed countries.

**Objectives:** The present review aimed to explore the differences among the reports on number and age standardized incidences of CRC in both sexes in different areas of Iran to find the incidence trend of this cancer.

**Data Sources:** All the published reports citing the incidence of CRC in Iran were collected by conducting a literature search in international databases.

**Study Selection:** English articles were included where there was a clear definition of the population of patients under study and where the criteria for diagnosing CRC were well described.

**Data Extraction:** One author read each paper and extracted several studies and then the studies suitable for inclusion were reported in three categories.

**Results:** We identified 181 independent studies dating back to 2003; 168 full text articles were assessed for eligibility. However, 136 full text articles were excluded due to different reasons. Finally, 26 studies were suitable for inclusion in the analysis. The highest and lowest (age standardized rates) ASRs were respectively 3.4 and 2.6 in males and 11.42 and 10.56 in females. Time showed a slightly increasing trend in recent years.

**Conclusions:** Although Iran was expected to have a low incidence rate of CRC, recent studies revealed a slightly increasing trend for the incidence rate of CRC. This finding shows the necessity to consider CRC screening as an important issue in health policy priorities.

**Keywords:** Iran; Colorectal Neoplasms, Colon; Administration, Rectal; Incidence

## 1. Context

Colorectal cancer (CRC) is the third most prevalent cancer worldwide which is less common in the Middle East. It is also the second leading cause of cancer-related mortality and represents a major public health problem in developed countries (1). CRC is an important public health problem with nearly one million new cases diagnosed worldwide and half a million deaths annually (2). Due to the high incidence and mortality rates in western populations, CRC has been extensively studied in these countries. The highest rates are related to developed countries, including the US, Canada, Australia, and North-Western Europe (3, 4). Yet, a comparatively low rate has been observed in Asian, African and South American countries. Of course, the incidence rates are increasing in the countries that were previously considered to have low incidence. Overall, the incidence and mortality rates of CRC vary markedly around the world (4). Globally, CRC is the third most commonly diagnosed cancer in males and the second in females (5). In the US, both the inci-

dence and mortality rates have been slowly but steadily decreasing. Annually, approximately 50830 Americans die of CRC, accounting for approximately 9% of all cancer deaths. In the US also, the CRC incidence rates have declined by about 2-3% per year over the last 15 years. The incidence rates in most other western countries have been stable or increased slightly during this period (6).

However, information regarding CRC, in particular population-based data, is limited in Middle Eastern countries. Based on the World Health Organization (WHO)'s reports, CRC incidence rates have rapidly increased in several areas historically at low risk, including Asia and Eastern Europe. The incidence rate of CRC is also rapidly rising in some Asian countries such as China, Japan, South Korea and Singapore. These countries have experienced a 2-4-fold increase in the incidence of CRC during the past few decades (7). However, Iran is still a low-risk country for CRC, particularly among the older population (8). Although the age standardized rate (ASR) is close

in the young Iranian and the US population, the rates are much lower among older Iranians (9).

## 2. Objectives

The present review aimed to explore the differences among the reports on number and age standardized incidences of CRC in both sexes in different areas of Iran to find the incidence trend of this cancer.

## 3. Data Sources

All the published reports citing the incidence of CRC in Iran were collected by conducting a literature search in international databases, including Science Direct, Springer, PubMed, Elsevier, Emro, Cinhal, Proquest and Medline, as well as in Iranian databases including Iran Medex, Scientific Iranian Database, MagIran, Novin Pajouh, Islamic World Science Citation Center (ISC), and Iranian Research Institute for Information Science and Technology (Iran Doc), using the following keywords: colon OR colorectal OR rectum (prevalence OR frequency OR incidence) AND (cancer OR tumor OR carcinoma or carcinogen or pathogen) AND (Iran OR Persian). Thereafter, a comprehensive search of the reference lists of all the review articles and the retrieved original studies was performed to find the studies that were not identified by the Medline search. This identified 181 independent studies dating back to 2003.

## 4. Study Selection

English articles were included where there was a clear definition of the population of patients under study and where the criteria for diagnosing CRC were well described. However, the studies citing cancer mortality statistics (not incidence rates) were excluded as this is not a true representation of cancer incidence. Duplicate publications and the studies that obviously described the biological event or evaluated the risk factors of colon cancer and interventional studies were also eliminated. Articles related to the burden of the disease were excluded as well.

## 5. Data Extraction

One author read each paper and extracted several studies using a predefined review form which evaluated the methodological quality score for prevalence studies (see appendix). Every article with a score below eight was excluded from the analysis.

The studies suitable for inclusion were reported in three categories:

- 1) Number of total CRCs by sexual stratification.
- 2) Crude rate of total CRCs by sexual stratification.
- 3) Age standardized rates (ASRs) of total CRCs by sexual stratification.

## 6. Results

A total of 181 studies were identified, among which eight articles overlapped with other studies or includ-

ed the same patients. Out of these eight, five related to other cancers; therefore, they were excluded in the first screening. After these steps, 168 full-text articles were assessed for eligibility. However, 136 were excluded due to the following reasons: 63 provided details concerning biological situations, 41 related to the risk factors, 15 were interventional studies, five had been performed out of Iran, 12 related to the burden of the disease, and six had methodological quality scores below eight. This left 26 studies suitable for inclusion in the analysis (Figure 1). These studies had been conducted during 2003-2014. The smallest and largest studies had been conducted on 180 and 19617 subjects, respectively. In all the studies, ASR of the male patients was higher than that of the females.

Among the articles under investigation, seven studies related to all parts of Iran, five were performed in Tehran, and the remaining related to 12 provinces. Besides, 48% of the articles were only published in Asian Pacific Journal of Cancer Prevention. According to the results, the highest and lowest ASRs were respectively 3.4 and 2.6 in males and 11.42 and 10.56 in females. In the study performed by Safaee et al. (10) ASR was reported for the overall ASR in the four-year period from 2005 to 2009 (ASR for total = 23.25). Moreover, all the studies, except for the one conducted by Haghdoost et al. (11) and Golfam et al. (12) demonstrated that the number of male patients was higher than that of females. Only in two studies performed in Kerman province, ASR of CRC was higher in females compared to males. In all the cases, ASR was higher than the crude rate. The difference between male and female ASRs varied from 0 to 4.1. Furthermore, time showed a slightly increasing trend (Table 1).

## 7. Conclusions

In this study, the incidence rate of CRC and its geographical variation across Iran was systematically reviewed for the first time. Although this region was expected to have a low incidence rate of CRC, recent studies revealed a slightly increasing trend for that. This finding showed the necessity to consider CRC screening as an important issue in health policy priorities. CRC is the fourth most common cancer in males (3811 cases, 8.5% in total) and the second in females (3352, 8.4% in total) in Iran (2). There is a wide geographical variation in the incidence rate of CRC across the world and the geographical patterns are very similar in males and females. In addition, almost 55% of the cases occur in more developed regions. Our findings also showed that the variation between the incidence rates across Iran was very similar in males and females.

According to the results, the highest estimated rates related to Australia/New Zealand (ASR 44.8 and 32.2 per 100000 in males and females, respectively), while the lowest rate related to Western Africa (4.5 and 3.8 per 100000 in males and females, respectively) (2). In Iran, the variation between reports of ASR for CRC in different studies was within the acceptable range. In the study by Safaee et al. (10) reporting the overall ASR in a four-year

period, the incidence rate of CRC was relatively high in Iran compared to other Asian countries (37, 38).

Although we could not depict any obvious time trend among different published studies, recent studies somehow showed a higher ASR compared to the previous ones. On the other hand, many Asian countries, including China, Japan, South Korea and Singapore, have experienced a 2-4-fold increase in the incidence of CRC during the past few decades. The rising trend of the incidence and mortality rates of CRC is more striking in affluent than in poorer societies and differs substantially among ethnic groups. Although changes in dietary habits and lifestyle are believed to be the reasons underlying this increase, the interactions between these factors as well as the genetic characteristics of Asian populations might also have a pivotal role. In addition, the prevalence of CRC risk factors was high in Iran and its trend was still growing up (39). A comparison of age-specific rates between Iran and the US showed similar rates in young (< 40 years) Iranians and Americans, but much lower rates among older ( $\geq 40$ ) Iranians (14). Therefore, evidence showed an increasing trend of CRC in recent years. Besides, ASR of the male patients with CRC in Tehran was higher than that reported in Pakistan and Turkey, the neighboring countries

(40, 41). Although the figures for gastric and oesophageal cancers were decreasing, the incidence of CRC followed an increasing trend (28). This evidence can in fact be a warning and it might be necessary to screen for CRC or consider this issue in health policy priorities.

In most cases, ASR of the male patients with CRC was higher compared to those of females, which was probably due to the higher prevalence of inflammatory bowel diseases in males (42). However, gender disparity was not considerable in this study which could be due to similarity of the etiologic factors in both sexes. Moreover, although high risk behaviors such as smoking, alcohol consumption and drug abuse are more common in males, Iranian females are exposed to a major risk factor for CRC, i.e., inactivity. Furthermore, the nature of this disease in our country may be genetic rather than environmental and can affect both sexes equally (10).

According to the reported studies, the lowest ASR of CRC related to the south-west of Iran, including Kerman, Fars and Khuzestan provinces, while the highest ASR was related to north-west of the country, including Golestan, Guilan and Kermanshah provinces. This trend has also been found for stomach and oesophageal cancers in Iran (43).

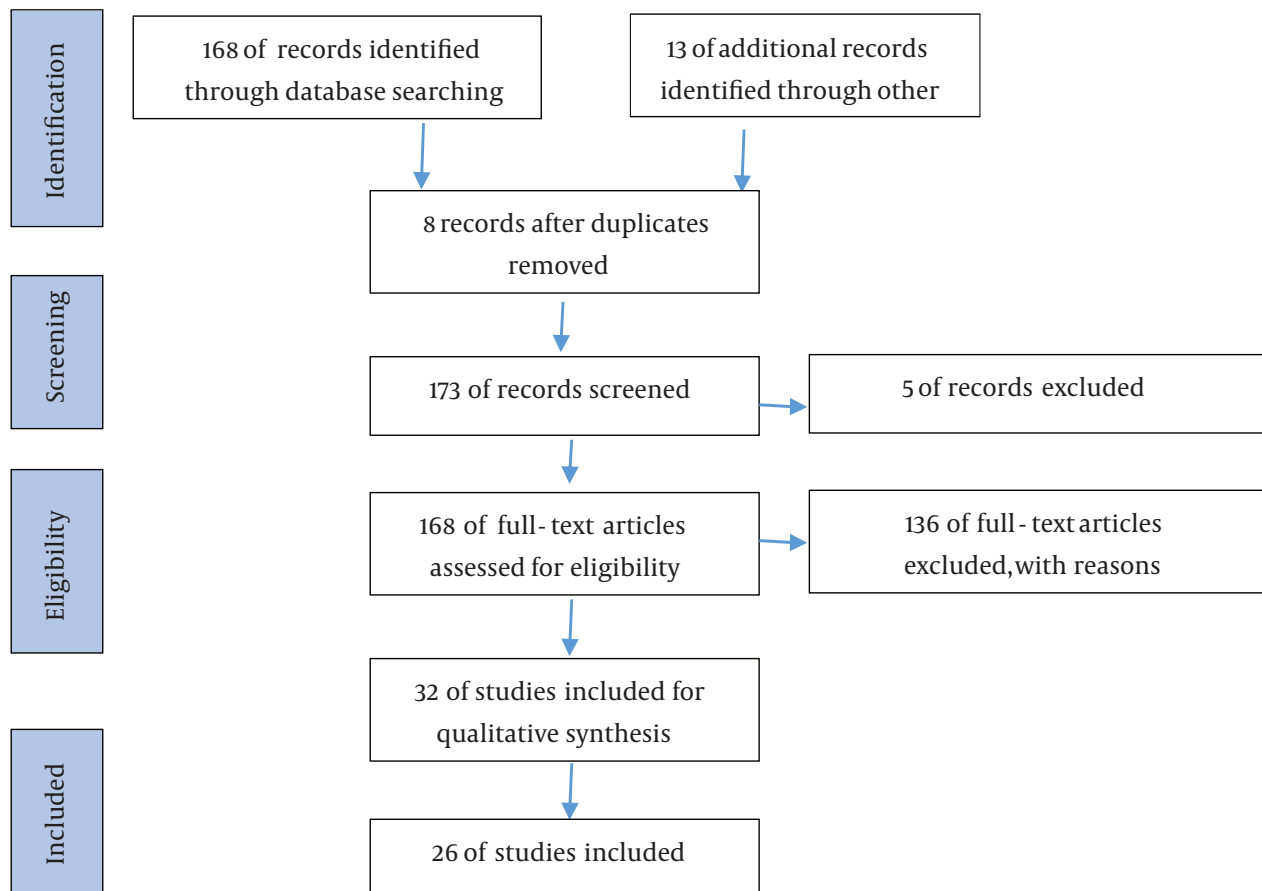


Figure 1. PRISMA Flow Diagram

**Table 1.** Summary of the Articles Published on the Incidence of Colorectal Cancer in Iran <sup>a</sup>

Number	Year	Location	Authors	Journal	Total CRC, No.	CRC in Males, No.	CRC in Females, No.	Crude rate of Total CRC	Crude rate of Males With CRC	Crude rate of Females With CRC	ASR of Total CRCs	ASR of CRCs in Males	ASR of CRCs in Females
1	2005	All provinces	Sadjadi et al. (13)	APJCP	3641	2046	1595	-	-	-	-	8.3	6.5
2	2006	All provinces	Ansari et al. (14)	Cancer Letters	-	-	-	-	-	-	-	8.2	7.0
3	2006	All provinces	Yavari et al. (15)	APJCP	-	-	-	-	-	-	-	11.6	10.1
4	2008	All provinces	Yavari et al. (16)	APJCP	644	385	259	-	-	-	-	-	-
5	2008	All provinces	Esnaashari et al. (17)	Pajohesh dar Pezeshki	4156	2211	1945	-	-	-	-	6.09	4.54
6	2009	All provinces	Mousavi et al. (18)	Annals of Oncology	4056	2255	1801	-	6.37	5.36	-	8.19	7.56
7	2012	All provinces	Azadeh et al. (19) <sup>b</sup>	APJCP	19617	10991	8626	-	-	-	23.55	39.96	36.16
8	2003	Ardabil	Sadjadi et al. (20)	Int. J. Cancer	180	106	74	-	5.04	3.33	-	7.86	5.89
9	2006	Ardabil	Ansari et al. (14)	Cancer Letters	190	116	74	-	-	-	-	7.9	5.9
		Guilan	Ansari et al. (14)	Cancer Letters	586	293	293	-	-	-	-	7.8	7.4
		Mazandaran	Ansari et al. (14)	Cancer Letters	536	297	239	-	-	-	-	9.9	8.4
		Golestan	Ansari et al. (14)	Cancer Letters	380	241	139	-	-	-	-	10.7	6.6
		Kerman	Ansari et al. (14)	Cancer Letters	341	182	159	-	-	-	-	6.4	6.2
		All provinces	Ansari et al. (14)	Cancer Letters	2033	1129	904	-	-	-	-	8.2	7.0
10	2005	Kerman	Pahlavan et al. (21)	Tumori	378	199	179	-	3.9	3.6	-	5.9	5.9
		Ardabil	Pahlavan et al. (21)	Tumori	180	106	74	-	5.0	3.3	-	7.86	5.89
		Mazandaran	Pahlavan et al. (21)	Tumori	688	383	305	-	8.9	7.0	-	9.9	8.4
11	2012	Guilan	Joukar et al. (22)	Int J Clin Exp Med	904	615	289	-	-	-	-	-	-
12	2013	Guilan	Atrkar-Roushan et al. (23)	APJCP,	2633	1402	1231	5.36	-	-	5.45	-	-
13	2014	East Azerbaijan	Somi et al. (24)	APJCP	366	201	165	-	-	-	-	11.2	8.93
14	2013	Fars	Talaiezhadeh et al. (25)	APJCP	-	-	-	-	-	-	-	3.4	2.6
15	2012	Golestan	Roshandel et al. (26)	AIM	611	345	266	-	8.34	6.54	-	12.4	9.5
16	2013	Golestan	Talaiezhadeh et al. (25)	APJCP	-	-	-	-	-	-	-	12.4	9.5
17	2013	Kerman	Roya (27)	APJCP	792	413	379	-	-	-	-	-	-
18	2011	Kerman	Haghdooost et al. (11)	IJCP	551	275	277	2.1	2.1	2.2	5.1	5.0	5.3
19	2011	Kermanshah	Najafi et al. (28)	IRCMJ	394	232	162	-	-	-	4.5	-	-
20	2013	Kermanshah	Abdifard et al. (29)	APJCP	-	-	-	-	-	-	6.2	7.7	4.7
21	2013	Khuzestan	Talaiezhadeh et al. (25)	APJCP	1102	627	475	-	4.32	3.45	-	6.32	5.72
22	2008	Mazandaran and Golestan	Mohebbi et al. (30)	BMC Cancer	1034	556	478	-	-	-	-	4.88	4.32
23	2004	Shiraz	Hosseini et al. (31)	ANZ J Surg.	-	-	-	-	-	-	-	4.2	2.72
24	2005	Semnan	Babaei et al. (32)	APJCP	-	-	-	-	10.6	8.4	-	11.42	10.52
25	2005	Tehran	Emami et al. (33)	Govaresh	952	540	412	2.1	-	-	-	-	-
26	2008	Tehran	Azadeh et al. (19)	APJCP	1138	696	442	-	-	-	-	-	-
27	2009	Tehran	Khabazkhoob et al. (34)	Gorgan University Journal	-	-	-	-	4.3	4	-	5.7	5.4
28	2012	Tehran	Rohani-Rasaf et al. (35)	APJCP	-	-	-	-	-	-	-	8.9	7.3
29	2013	Tehran	Golfam et al. (12)	IRCMJ	218	78	140	-	-	-	-	-	-
30	2012	West Azerbaijan	Mahmodlou et al. (36)	ISRN Gastroenterology	546	306	240	-	-	-	-	-	-

<sup>a</sup> Abbreviation: CRC, colorectal cancer.<sup>b</sup> The overall ASR in the four years period (2005-2009).

The present analysis indicated a slight difference between the reported incidence of CRC in most studies and the estimated cancer incidence for Iran by GLOBOCAN in 2012 (ASR: 11.6 for males and 10.5 for females) (2). GLOBOCAN database uses a large amount of data derived from cancer registries from different national populations or subsamples from selected regions. On the other hand, the national cancer registry in 2009 reported ASR for males and females to be 11.31 and 5.88, respectively (8). This remarkable difference can be justified because pathology-based cancer registry underestimates the cancer incidence and cannot be a reliable source for policy making and research (44). Therefore, further investigations in other provinces may help for mapping out the real incidence rate of cancer in Iran.

One of the limitations of our study was that it was a systematic review of ecological studies; thus, the quality of the data may be in question. Besides, cancer epidemiological studies in developing countries such as Iran are limited by the dearth of tools for disease control and surveillance. In addition, most of the studies were localized in a special part of Iran and half of the articles had been published in only one journal. Hence, the obtained results cannot be generalized and the quality of these studies may not have been suitable.

## Authors' Contributions

Abbas Rezaianzadeh: primary idea and final approve. Ali Reza Safarpour: revision and data collection. Maryam Marzban: writing and design of the manuscript. Abdolmohammad Mohaghegh: revision and data collection.

## Funding/Support

Shiraz University of Medical Sciences, Shiraz, IR Iran supported this study.

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