REVIEW ARTICLE



Incidence and Risk Factors of Colorectal Cancer in the Iranian Population: a Systematic Review

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Abstract

Purpose Colorectal cancer (CRC) is one of the most common cancers in the world. The aim of this study was to investigate its incidence and risk factors in the Iranian population.

Methods A literature search was conducted in PubMed, Web of Science, Scopus, SID, and Magiran from inception until 2019. Studies that reported the incidence rate and risk factors of colorectal cancer were included in this review.

Results Twenty-one articles that reported the incidence rate and 13 that reported the risk factors were included. The incidence rate was different according to the population type, gender, age, and study year in different regions. The main risk factors for colorectal cancer were high consumption of red meat and fried food and low intake of fruits and vegetables, diabetes, a positive family history, and obesity.

Conclusion The incidence of CRC has a marked variation in different parts of Iran, and various risk factors are associated with colorectal cancer. According to incidence rate and various risk factors, precise planning is needed to control colorectal cancer in the future.

Keywords Colorectal cancer · Incidence rate · Risk factors · Iran

Abbreviations

CRC Colorectal cancer

ASR Age-specific incidence rate WHO World Health Organization

NOS Newcastle-Ottawa quality assessment scale

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Introduction

Colorectal cancer (CRC) is one of the most common and important cancers in the world. According to GLOBOCAN and the World Health Organization, 1.8 million new cases and 880,792 deaths related to CRC were reported in 2018 [1, 2]. The incidence of CRC has changed dramatically worldwide, with the highest rates seen in parts of Europe (such as Slovakia, the Netherlands, Norway, and Hungary). The agespecific incidence rate (ASR) is up to 60 per 100,000 in men and up to 35 per 100,000 in women [3]. The ASR is 2 to 3 times lower in Asia than in Europe [3]. The global burden of CRC is increasing rapidly with population growth and demographic and lifestyle changes, making CRC the third most common cancer and the fourth leading cause of cancer death in the world [1, 4]. CRC is more common in men than in women and is 3 to 4 times more common in developed versus developing countries [5]. Among Iranians, CRC is the third and fourth most common cancer in men and women, respectively [6]. CRC is a multifactorial disease with several risk factors including genetic factors, dietary pattern (such as low intake of fruits and vegetables), smoking and alcohol consumption, obesity, stressful life events, hormonal factors,



and low physical activity [1, 7, 8]. About 10–15% of CRC cases are genetic that are generally more common in the elderly [8]. Information on the incidence rate and risk factors of CRC is necessary for planning to reduce the burden of this cancer. Because of limited information on CRC, and regarding rapidly increasing incidence rates in several areas that historically at low risk, based on the World Health Organization (WHO)'s reports, including Asia and Eastern Europe, this systematic review used a comprehensive literature search to determine the incidence and risk factors of CRC in the Iranian population.

Methods

Search Strategy

For a systematic investigation, Persian (national) and English (international) electronic databases were searched. The included databases were PubMed (MESH terms), Web of Science, Scopus, SID, and Magiran from inception to 2019. The following keywords were used: risk, population at risk, risk factors, prognostic factors, colorectal neoplasm, colorectal cancer, epidemiology, and Iran. Totally, the search yielded 441 and 290 publications for incidence rate and risk factors of colorectal cancer, respectively. Initially, two authors reviewed the titles and abstracts. The inclusion criteria were articles published in Persian or English and original studies that investigated the incidence rate and risk factors of colorectal cancer in Iran. In addition, letters to the editor and case reports were excluded. Moreover, articles published in languages other than English or Persian were excluded. A total of 264 duplicates and irrelevant articles were removed. The remaining 467 articles were reviewed by title and abstract. Afterward, 85 articles were reviewed by full text. Consequently, after reviewing the full texts, 37 and 14 articles were found to be irrelevant in terms of incidence rate and risk factors of colorectal cancer, respectively. After excluding these articles, 21 and 13 full texts were included and examined by two authors (Figs. 1 and 2).

Quality Assessment

The quality of studies was assessed using the Newcastle-Ottawa quality assessment scale (NOS) adapted for observational studies [9]. The NOS is based on three domains, including the selection of study groups, comparability of groups, and description of exposure and outcome. This scale assesses the quality of each study in each domain using eight items and a star scoring system. All items except the comparability domain have one star (the comparability domain has a maximum score of two stars). Totally, the earned stars are calculated as the total quality score for each study. A cut-off score of 6 or

higher was considered as high quality. Two reviewers completed quality assessment independently. In cases of disagreement or for items that remained unclear, a third reviewer was consulted.

Data Collection and Analysis

Two reviewers (FKH and HMS) screened the titles and abstracts to identify the studies that met the inclusion criteria. The studies were selected independently, and the results were discussed to make the final selection. A final decision was made for each study after reading its full text. In cases of disagreement, a third reviewer was consulted.

Data Extraction

We used a structured form to extract the data, including the study type and sample size, study place, incidence rate, risk factors, and protective factors of colorectal cancer. The same reviewers who selected the studies performed data extraction. All disagreements were discussed with a third reviewer, if necessary.

Results

The Characteristics of Included Studies

The results of the systematic search and article selection stages are shown in Figs. 1 and 2. The search yielded 731 studies, of which 264 duplicates were excluded. The remaining studies were assessed by title and abstract, resulting in the exclusion of 381 studies. Full-text screening was performed for 85 studies; finally, 34 articles meet the inclusion criteria. From included studies, 21 studies were cross-sectional, 10 case-control, 2 prospective, and 1 study retrospective. Moreover, 7 studies were conducted based on cancer registry data for all country, and all other studies used provincial data. Regarding the language of studies, 23 studies were in English and 11 in Persian.

Quality of Studies

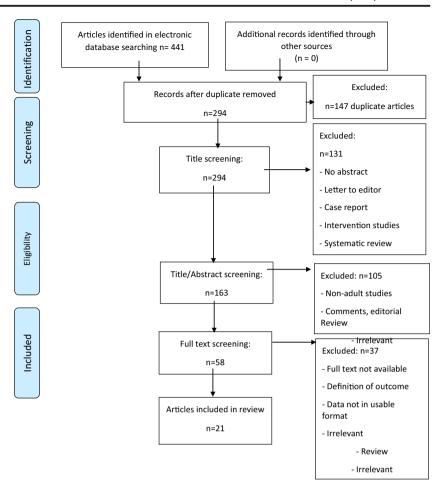
Based on the Newcastle-Ottawa quality assessment scale (NOS) for observational studies for incidence rate, 17 articles were of moderate to high quality, and 4 were of poor quality. Based on risk factors, 10 articles were of moderate to high quality, and 3 were of poor quality.

Incidence Rate

Twenty-one articles were selected for incidence rate. The algorithm of selecting the studies and their characteristics are



Fig. 1 Flow chart depicting the study selection process (incidence rate)



presented in Fig. 1 and Table 1, respectively. The incidence rate of colorectal cancer has been shown in different regions of Iran. The incidence rate was different according to the population type, gender, age, and study year in different regions. In women the lowest standardized incidence of CRC was in Fars province (2.41% per 100,000), and the highest standardized incidence was in East Azerbaijan (43.51% per 100,000). In men the lowest standardized incidence of CRC was in Fars province (3.26% per 100,000), and highest standardized incidence was in East Azerbaijan (63.02% per 100,000). Also standardized incidence was higher in the elderly than in the young and has increased over time in many studies. Table 1 shows the results of 21 studies reporting the incidence rate in different cities and population in Iran.

Risk Factors

Thirteen articles were selected for risk factors. The algorithm of selecting the studies and their characteristics are presented in Fig. 2 and Table 2, respectively.

Table 2 shows the results of 13 studies reporting the risk factors of CRC in different Iranian cities and populations. Risk factors were different in different regions of Iran, although

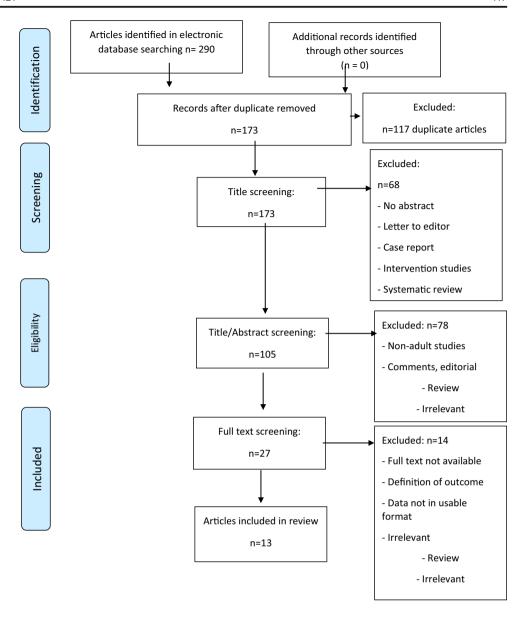
some factors have a protective role against cancer. The main risk factors of CRC were high consumption of red meat and fried food and low intake of fruits and vegetables, diabetes, a positive family history, and obesity. Protective factors that have been shown in various studies to play a role in the prevention of CRC include level of education and literacy of individuals, consuming fruits and vegetable, and physical activity.

Discussion

This review study was conducted to determine the incidence of colorectal cancer in different regions of Iran. The incidence rate varied in different regions according to the population type, gender, age, and study year. This variation may be related lifestyle and diet [13]. Moreover, the high prevalence of obesity, low physical activity, dietary habits, and certain lifestyles in different regions can explain the difference in the incidence of colorectal cancer between different regions of Iran [42]. The high incidence of this cancer in young people in some areas can be attributed to diet and lifestyle favoring a Westernized pattern. Lifestyle and diet modification may help



Fig. 2 Flow chart depicting the study selection process (risk factors)



to reduce the burden of the disease in areas with a high incidence [42]. The incidence of colorectal cancer was higher in men than in women. One of the reasons that can explain this trend is that women are more sensitive to their health than men are and present to health centers with the smallest signs of illness to receive treatment, so the disease can be diagnosed and treated in the early stages [14]. According to the results, the prevalence of CRC is on the rise in both genders. Regardless of the demographic characteristics of individuals, part of this increase could be due to improvement in cancer registration in Iran [17]. Improved life expectancy in the country and population aging can be other causes for this increase.

This study showed an association between several risk factors and colorectal cancer; however, these risk factors may vary in different countries. Low consumption of fruits and vegetables is one of the main risk factors of CRC. It is

reasonable to assume that fiber, fruits, and vegetables reduce the density of carcinogens as well as the contact time of carcinogens with the gastrointestinal tract, which can prevent colorectal cancer. Some fruits such as the orange and lemon and vegetables contain vitamin C, vitamin B, and antioxidants and reduce the incidence of colorectal cancer [8]. Genetic factors also play a role in colorectal cancer. Genetic sensitivity can affect every stage of the cancer, including modifying the effect of environmental carcinogens [38]. One of the factors that is related to colorectal cancer is the use of opioids. A suggested mechanism for the relationship between opium use and cancer is that opium and its alkaloids, including morphine, may have mutagenic effects. Some of the impurities added to opioids during their processing in Iran may have carcinogenic effects. One of these materials is lead, which is added to make it heavier [39]. Furthermore, a relationship was



 Table 1
 General characteristics of the studies about incidence rate of colorectal cancer

| Row | First author | Year | Type of study | Number of participants | Place of study | ASR (per 100,000 persons) | Source |
|----------|---------------------------|----------|---|---|--|--|-------------|
| _ | Saeid Razi | 2015 | Cross-sectional | In 2003: 1296 | Iran (Concon Dominton Acto) | The lowest in 2003: 5.47 | [10] |
| 2 | Dr. Nahid Khademi | 2014 | Cross-sectional (women) | III 2008: 2638 2009: 1976 2010: 2233 | (Cancer registry data) Kermanshah | The ingress in 2008; 11.12 In 2009; 7.8 In 2010 8 7 | [11] |
| 3 | Najibullah Baraadeh | 2015 | Cross-sectional | 5617 | Khorasan Razavi | 7.5 in women | [12] |
| 4 | Reza Ansari | 2006 | Cross-sectional | 2033 | Iran | 7.5 III women 8.2 in men | [13] |
| | | | | | (Cancer Registry data) | 7 in women | |
| ı | | 7100 | - | | | The highest in males in Golesian: 10.7 The highest in females in Mazandaran: 8.4 | Ş |
| n | Zemab Almasıl | 2016 | Cross-sectional | /163 | Iran (Cancer Registry data) | 11.1 | [14] |
| 9 | Mehrabani | 2008 | Cross-sectional | In men: 112 In women: 85 | Fars Province | In men: 3.26 | [15] |
| 7 | Gholamreza Roshandel | 2014 | Cross-sectional | In men:345 | Golestan Province | In wonen: 2.41 In males 12.4 | [16] |
| ∞ | Mehri Rejali | 2018 | Cross-sectional | In women: 266 2902 | Isfahan | In females 9.5 In 2000: 3.47 | [17] |
| | , | | | | | In 2011: 10.22 | , |
| 6 | Somi | 2009 | Cross-sectional | In men: 78 | East Azerbaijan | In men: 63.02 | [18] |
| 10 | Mohammad Hossein Somi | 2014 | (in people over 65 years of age) Cross-sectional | In women: 47 In women: 2540 | East Azerbaijan | In wonen: 45.51 In men: 11.2 | [19] |
| = | Edris Abdifard | 2013 | Cross-sectional | 292 | West of Iran | In women: 8.93 Minimum 1 5 in 2000 | [20] |
| : | rans voanaa | 6107 | (1035-30010m | | 10 CO 10 Heat | Maximum 4.8 in 2005 | 5 |
| 12 | Neda Amoori | 2014 | Cross-sectional | 14,893 | Khuzestan Province of Iran | In males 11.6 | [21] |
| 13 | H.A. Nikbakht | 2015 | Cross-sectional | 237 Patients | Babol City | III remares 10 In 2007: 7.7 | [22] |
| 7 | Makenagad Malrili | 2017 | Concident | 4631 | Vond | In 2012:14.6 | [22] |
| ±. | Mallillood Vakili | † 102 | Closs-sectional | 1031 | i azu | The lowest in relates in 2006: 5.1 The lowest in females in 2006: 5.1 The highest in males in 2009: 9.9 The lowest in males in 2007: 6.1 | [67] |
| 15 | Amori | 2017 | Retrospective study | 301,055 | In Iran | In males 8.29 | [24] |
| 71 | Mahdi Damhi | 2010 | Louis House Steel | L- 2001 | Designation of the Minister of Its | In females 7.75 | [36] |
| 10 | Mellal Dalaoi | 2010 | Cross-sectional | In 2001 In men: 379 In women: 344 In 2010 | registation of the Ministry of reguli In Iran | 2010 in males it was 11.28 in males and 10.33 in women | <u>[3</u>] |
| | | | | In men: 3443 In women: 2641 | | | |
| 17 | Fatemeh Khosravi Shadmani | 2017 | Cross-sectional | 6185 | Iran | The highest in males in Tehran: 20.58 | [26] |
| <u>×</u> | Seved Vahid Hosseini | 2004 | Cross-sectional | In the 1970s to 80s: 64 | (National Cancer Registry) Shiraz | The highest in females in Guilan: 20.48 In males from 1970s to 1980s 1 9 to 4.2 | 1271 |
| 2 | | | | In the 1990s to 2000s: 264 | | In females from 1990s to 2000, 2.35 to 2.72. | Ī. |
| 19 | Marzieh Rohani-Rasaf | 2017 | Cross-sectional | In people over 65: 3104 | Tehran | In people over 65: 86.13 | [28] |
| 20 | Seyed Masoom Masoompour | 2016 | Cross-sectional | In men: 5594 In women: 4628 | Fars province | 7.49 | [29] |
| 21 | Edris Abdifard | 2016 | Cross-sectional | 36,650 | Iran (National Cancer Registry System) | In men, in 2000: 1.6 in 2009: 11/3 In women, in 2000: 1.6 | [30] |
| | | | | | | in 2009; 10.9 | |



 Table 2
 General characteristics of the studies about risk factors of colorectal cancer

| Row | Row First author | Year | Year Place of study | Type of study | Number of participants Risk factor(s) | kisk factor(s) | Protective factor | Source |
|-----|--------------------------------------|-----------|---------------------|-------------------------------------|---------------------------------------|---|-------------------------|----------|
| | Naeimeh Keyghobadi | 2013 Yazd | Yazd | Case-control | 60 case F | High consumption of red meat and fruit | | [31] |
| 7 | Hossein Azizi | 2014 | 2014 Tabriz | Case-control | | Diabetes | | [2] |
| 3 | Ali Ahmadi | 2014 | 2014 Mazandaran | Prospective investigation | 207 conuoi 1127 | Consumption of fight fat and red fileat Old age | Level of education and | [32] |
| | | | | | 5 7 H | Smoking Family history of colorectal cancer | literacy of individuals | |
| 4 | Kamran moshafaghi | 2010 | | Case-control | | Lower education | | [33] |
| | | | | | 140 control I | Living rental home History of the disease in family Red meat | | |
| | | | | | | Daily intake of dairy products High-fat diet | | |
| | | 6 | | • | | History of laxative Use and history of gastrointestinal diseases | | |
| S | Azadeh Satayee | 2009 | 2009 Tehran | Case-control | 393 case F 393 control | Family history | | [34] |
| 9 | Shadi dehghanzadeh | 2012 | 2012 Rasht | Case-control | | BMI | Consuming fruits | [35] |
| | | | | | 150 control I | Inflammatory bowel disease History of polyp Diabetes | Vegetable | |
| | | | | | 0 02 | Consuming red meat Smoking cigarettes | | |
| 7 | Abbas Ali Keshtkar | 2009 | 2009 Golestan | Case-control | 47 case F | Frying food Fat consumption | | [36] |
| ∞ | Ali Hosseinzadeh | 2011 | 2011 Esfahan | Case-control | | Increased total energy consumption Use of high-fat diet | Physical activity | [37] |
| | | | | | |) | , | 1 |
| 6 | Hedayat Abbastabar | 2015 Iran | Iran | Ecological study Cross-sectional | 89,404 individuals I | Diabetes mellitus hypertension lacking or low physical activity | | ∞ |
| | | | | | 1 | High education high intake of dairy products non-consumption of vegetables and fruits | | |
| 10 | Saeideh Ebrahimkhani | 2012 | 2012 Tehran | Case-control | 100 case (| Genetic factors | | [38] |
| 11 | Ahmad NAGHIBZADEH-TAHAMI 2016 Kerman | 2016 | Kerman | Case-control | | Opioids | | [39] |
| 12 | Anahita Nosrati | 2016 Sari | Sari | Case-control | | Genetic factors | | [40] |
| 13 | Mohammad Movahedi | 2015 Iran | Iran | Prospective investigation | 937 participants | Obesity Body mass index | | [41] |
| | | | | | | | | |



found between family history and colorectal cancer. Increased risk of cancer in first-degree relatives of cancer patients may be explained by a common genetic or environmental factor during a specific time. In general, it is not possible to clearly distinguish between the environmental and genetic components in a susceptible family. Identification of the family history of colorectal cancer is important for prevention and management. In other words, evaluation of the first-degree relatives of CRC patients may result in detecting more people who are at risk for this cancer [34].

Our study has several limitations. First, most of the studies in this review are cross-sectional and case-control, and we need stronger studies such as cohort reviews to obtain more evidence in the future. Second, this study has been conducted in Iran, and in order to more accurately study the risk factors and identify the most dangerous areas of the world, a world-wide study will be needed.

Conclusion

The incidence rate of CRC was different according to the population type, gender, age, and study year in different regions. Also risk factors were different in different regions of Iran, although some factors have a protective role against cancer. The main risk factors of CRC were high consumption of red meat and fried food and low intake of fruits and vegetables, diabetes, a positive family history, and obesity. According to incidence rate and various risk factors, precise planning is needed to control colorectal cancer in the future.

Authors' Contributions Farzad Khodamoradi and Hossein Mozafar Saadati had the idea for the article. Farzad Khodamoradi and Hossein Mozafar Saadati performed the literature search and data analysis. Farzad Khodamoradi and Hossein Mozafar Saadati and Batool Okhovat drafted and/or critically revised the work.

Data Availability This study is a review study.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Code Availability Not applicable.

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