

Trends in colorectal cancer in Iraq over two decades: incidence, mortality, topography and morphology

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BACKGROUND: Colorectal cancer (CRC) is mainly a disease of the elderly in the Western world, but its characteristics are changing globally. Iraq does not have a well established CRC screening program. Understanding trends of CRC incidence, fatality and the clinical features of CRC patients is vital to the design of effective public health measures; public awareness, screening, diagnosis and treatment strategies to meet the future demands.

OBJECTIVES: Determine trends in demography, incidence proportion, mortality, topography (primary tumor site) and morphology (histology) over two decades.

DESIGN: Registry-based study

SETTING: Iraqi National Cancer Registry (INCR) database

PATIENTS AND METHODS: We collected and analyzed data from CRC patients obtained from the INCR to calculate incidence and mortality proportion per 100 000 population for the period from 2000 to 2019. In addition to estimation, data were examined by anatomic location and morphological type.

MAIN OUTCOME MEASURES: Change in the incidence and mortality proportion, topography and morphology of CRC over 20 years.

SAMPLE SIZE: 20880 CRC patients ranging in age from 14-80 years.

RESULTS: The overall (males and females) CRC incidence proportion (CIP) increased from 2.28 to 6.18 per 100 000 population in 2000 and 2019, respectively, with an annual percentage change (APC) of 5.11%. The incidence proportion (IP) of CRC in patients from 20 to <50 years rose from 1.46 in 2000 to 4.36 per 100 000 population in 2019, which is an APC of 5.6%. The IP in patients older than 50 years rose from 12.7 to 40.59 per 100 000 population in 2000 and 2019, respectively, with an APC of 5.98%. The percentage of all CRC cases to all total malignancies in Iraq grew from 3.69% in 2000 to 6.5% in 2019. The CRC mortality proportion increased from 1.25 to 1.77 per 100 000 populations in 2010 and 2019, respectively, reflecting an APC of 3.54%. Anatomically, colon (C18) tumor represented 59.2% and 65.7% in 2000 and 2019, respectively. Rectal (C20) tumors were 37.2% in 2000 down to 31.4% in 2019, while rectosigmoid junction tumor (C19) were 3.6% in 2000 dropping to 2% in 2019.

CONCLUSIONS: CRC in Iraq is still a disease of the elderly and is rising in incidence and mortality in all age groups. This necessitates reconsidering health policy regarding CRC; public awareness, screening and management strategies to accommodate for these alarming changes.

LIMITATIONS: Data about stages, grades and molecular characterisations are not available in the INCR.

CONFLICT OF INTEREST: None.

Coleland and the United State) than some Asian and African states.³⁻⁵ For example, in 2018, the CRC incidence rate ranged from more than 36 to less than 5 per 100 000 population in the New Zealand and South Central Asian countries, respectively.⁵ However, the incidence rate is growing in the relatively low incidence countries.^{2,5} This change is probably related to the adoption of the Western lifestyle with the consumption of more meat and less fruits and vegetables and more sedentary behaviour.^{2,5} CRC is regarded as a human development index.^{2,5}

It is generally accepted that CRC is a disease of the elderly.⁶ In different parts of the world, there has been a decline in the incidence rate of CRC in people older than 50 years while the incidence rate has increased 1% to 3% per annum for people younger than 50 years, which is known as early onset CRC.^{7,8} In the USA, the risk of CRC in those born in the 1990s was double the risk for those born in 1950s.⁹ Of 2020 USA figures, 17 930 new cases and 3640 deaths will have been in individuals younger than 50 years.¹⁰ Anatomically, this rise is limited to the distal colon (1.3%) and rectum (1.8%).¹¹

The American Cancer Society (ACS) changed its screening recommendations in 2018 from the age of 50 years to 45 years for individuals at average risk, owing to the upsurge in incidence in young adults.¹² In addition, research by the ACS has found that people younger than 55 years are 58% more likely to be diagnosed with a late-stage disease than older adults, making cure more difficult.¹² These variable global trends regarding CRC incidence, demography, pathology and fatality reflect the fact that genetic and environmental factors are main players in CRC.¹³

To the best of our knowledge, no comprehensive study has been done on CRC demography, incidence and fatality in Iraq. Iraq started cancer registration in 1974 and adopted the CanReg3 program in 2000, which was updated in 2019 to CanReg5 2019, which was developed by the International Agency for Research on Cancer (IACR, Lyon, France).¹⁴ The cancer registry collects cancer data from governmental and private hospitals and laboratories from all governorates of Iraq. However, Iraq does not have a well established CRC screening program. Immunological fecal occult blood testing and colonoscopy are performed at tertiary centres on a case by case basis. Understanding trends in CRC incidence, fatality and the clinical features of CRC patients is vital to design effective screening programs, public awareness, and diagnosis and treatment strategies to meet the future directions.

PATIENTS AND METHODS

This registry-based study was conducted from 1 November 2020 to 1 May 2021. We extracted data on 20 880 patients with CRC for the period of 2000-2019 from the Iraqi National Cancer Registry (INCR) annual reports published by the Iraqi Ministry of Health/Iraqi Cancer Board that are freely available to the public through its website.¹⁵ The data that are utilised do not contain any personal information or information on the identification of subjects. Thus, according to Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", the study does not require any ethical approval or informed consent of the participants.

We collected data on age, sex, incidence and mortality rates, topography (primary site) and morphology (histopathological type) of CRC from INCR in an Excel sheet. Mortality data were available for the years 2010-2019. The topography and morphology (histopathological type) of the malignancies was coded by the INCR according to the International Classification of Diseases for Oncology, (ICDO-Third Edition).¹⁶ We included CRC cases with topography (primary site) codes of C18 (colon), C19 (rectosigmoid junction) and C20 (rectum) regardless of the morphological type.

There were no data on the stage and grade, survival rate or molecular status of two genes that have been associated with CRC (*KRAS* and *BRAF* mutations) in the INCR annual reports.

Graphs were generated, and statistical analysis was performed using GraphPad Prism version 8.0.2 for Windows (GraphPad Software, San Diego, California USA). Incidence and mortality proportions were calculated from INCR data per 100 000 population for that year. The crude incidence proportion (CIP) and crude mortality proportion (CMP) for CRC refer to the number of new cases and deaths of CRC per 100 000 population in one year for all ages and both sexes. Age-specific incidence proportions (ASIP) and sex-specific incidence proportion (SSIP) and sex-specific mortality proportion (SSMP) per 100 000 population pertain to age or sex in one year. We divided our population into six age groups (20-29, 30-39, 40-49, 50-59, 60-69 and >70 years) for calculation of ASIP. Patients who were younger than 50 years were called young adults with early onset CRC as defined.^{7,8}

The unpaired t test was used for the comparison of numerical variables between two groups. We used overall and annual percentage changes (APC) for differences in the frequency of the variables between 2000 and 2019. A value apart from zero is considered significant.¹⁷ Linear regression was used for the trend analysis.

Table 1. The clinicopathological characteristics of the study subjects (20 880 colorectal cancer patients) who developed the disease over the last 20 years from 2000-2019.

Age range (years)	14-80
Age groups	
<50 years	6969 (33.4)
>50 years	13911 (66.6)
Sex	
Male	11333 (54.3)
Female	9547 (45.7)
CRC CIP/10 ⁵ population	
2000	2.28
2019	6.12
All Cancer CIP/10 ⁵ population	
2000	52
2019	91.7
Overall percentage change in CIP between 2000-2019	
CRC	171
All cancer	76.3
CRC CMP/ 10 ⁵ population	
2010	1.25
2019	1.77
All Cancer CMP/10 ⁵ population	
2010	28.35
2019	28.0
Percentage change in CMP between 2010-2019	
CRC	41.6
All cancer	-1.24
CRC CMP/CIP	
2010	0.42
2019	0.29
Topography of the tumors (primary site)	
Colon (C18)	13774 (66)
Rectum (C20)	6379 (30.5)
Recto-sigmoid (C19)	727(3.5)
Morphology of tumors (histology)	
Adenocarcinoma	17268 (82.7)
Mucinous adenocarcinoma	593 (2.85)
Epithelial tumors	449 (2.15)
Carcinoid tumors	104 (0.5)
Other types or cases without histology report	2466 (11.8)

A *P* value <.05 was considered statistically significant.

The quality of the data was considered sufficient since we had mortality/incidence rate data for a ten-years period and more than 90% of the cases had histopathological reports.

RESULTS

Study populations characteristics

Iraq has a high population growth rate, with a projected population number of 24 085 457 in 2000 to 39 927 889 in 2019 with an APC of 2.56% (male:female ratio, 1.02:1, 2019 projected population).

There were a total of 20 880 cases of colorectal cancer (C18-C20) with an age range of 14-80 years from all the 18 Iraqi governorates that are registered at the INCR over the years from 2000-2019. There were only 101 CRC cases in the age group 14-19 years. CRC cases (*n*=20880) were more common in males (54.7%) than females (45.3%) and 68.2% of all the cases were 50 years and older while 31.8% were younger than 50 (**Table 1**).

The CRC CIP increased dramatically from 2.28 in 2000 to 6.18 per 100 000 populations in 2019 for an upsurge of 171%. All cancer CIP increased from 52 per 100 000 population in 2000 to 91.7 per 100 000 population in 2019 representing an overall rise of 76.3%. The CMP of CRC rose by 41.6% between 2010 and 2019. In contrast, all cancer CMP reduced slightly (1.24%) over the same period.

Most of the cases were located at the colon (C18, 66%) followed by the rectum (C20, 30.5%) while the rectosigmoid junction had the lowest frequency (C19, 3.5%) (**Table 1**).

The vast majority of the cases had adenocarcinoma (82.7%). Other histological types such as epithelial (2.15%), mucinous adenocarcinoma (2.85%) and carcinoid tumor (0.5%) were also present. No histological reports or other histology types were seen in 11.8% of the cases.

Incidence proportion of CRC and frequency compared to other cancers

CRC CIP increased from 2.28 to 6.18 per 100 000 population in 2000 and 2019, respectively (*P*<.0001, APC=8.6%) (**Figure 1A**). The linear regression analysis showed that CRC incidence was higher in males (**Table 2**); 2.5 and 6.28 per 100 000 in males in 2000 and 2019, respectively (*P* value <.0001, APC=7.6%), than in females; 2.00 and 5.63 per 100 000 females in 2000 and 2019, respectively (*P*<.0001, APC=9.1%). The percentage of CRC relative to all other cancers for both sexes

combined rose from 3.69% in 2000 to 6.5% in 2019 ($P<.0001$, $APC=3.8\%$) (Figure 1B, Table 2). In both sexes, CRC ranked seventh in 2000 while it was third in 2019. The proportion of CRC to all malignancies in males was 4.2% and 8% in 2000 and 2019, respectively ($P<.0001$, $APC=4.5\%$) (Figure 1B, Table 2). It ranked seventh in 2000 and became the third in 2019. CRC had a relatively lesser contribution to total cancer in females from 3.58% to 5.33% in 2000 and 2019, respectively ($P<.0001$, $APC=2.6\%$) (Figure 1B, Table 2). CRC in females was the seventh most common tumor in 2000 becoming the fourth in 2019.

Age-specific incidence proportion (ASIP) over 20 years

The ASIP for CRC in patients from 20 to <50 years old increased from 1.46 to 4.36 per 100000 population in 2000 and 2019 with APC of 9.9% (Figure 2A). People older than 50 years had a rise of ASIP from 12.7 to 40.6 per 100000 populations in 2000 and 2019, respectively, with an APC of 10.98% (Figure 2B). The percentage change between the two groups was not statistically significant (Table 3). In the age group 20-29 years, the ASIP rose from 1.7 in 2000 to 2.79 per 100000 in 2019 with APC 3.2%, while the age group 30-39 years had an average annual increase of 6.3% increasing the ASIP from 3.7 to 8.24 per 100000 population in 2000 and 2019, respectively. The age group 40-49 years had an annual percentage change of 9.8%, with ASIP rising progressively from 7.7 to 22.86 per 100000 over 20 years. The age group 50-59 years had an ASIP of 22.32 and 50.20 per 100000 population in 2000 and 2019, respectively, with an APC of 6.2%. Yet the age group 60-69 years had the highest ASIP of 35 and 100 per 100000 population in 2000 and 2019, respectively, with APC 9.2%. For the age group ≥ 70 years, the incidence grew yearly by 6.25% from 38 to 78 per 100000 population over 20 years. Linear regression statistical

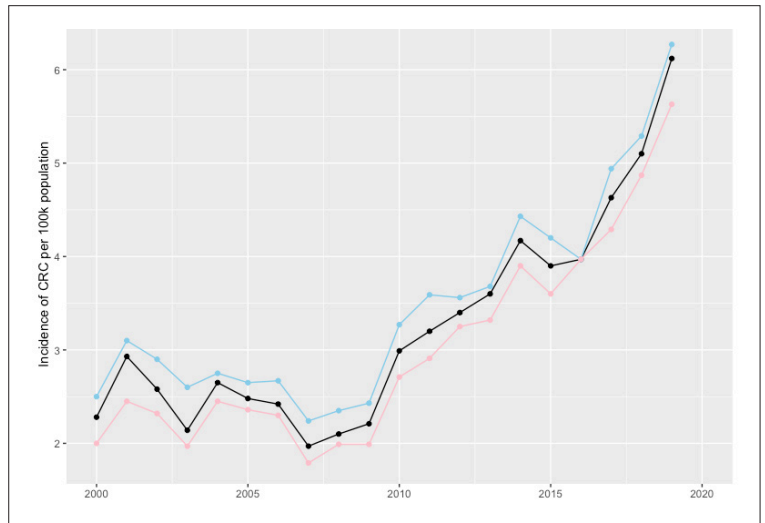


Figure 1A. Incidence of colorectal cancer per 100000 population (Both sexes=black, Male=blue, Female=pink).

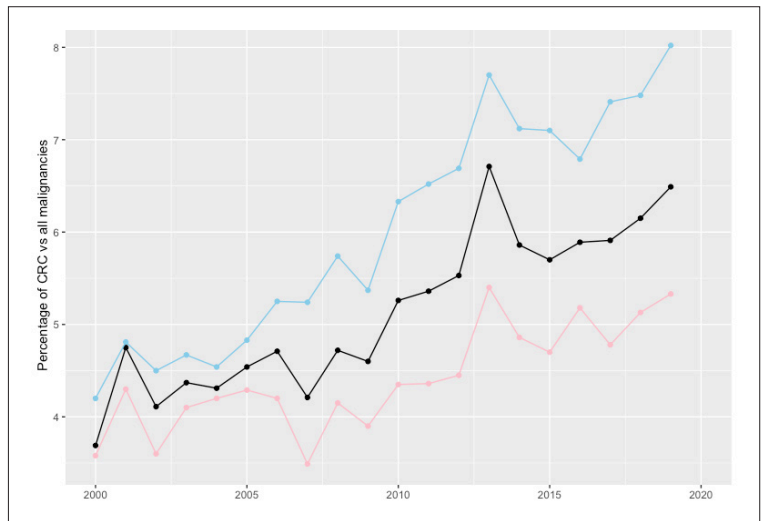


Figure 1B. Percentage of colorectal cancer compared to other malignancies (Both sexes=black, Male=blue, Female=pink).

Table 2. Linear regression statistical analysis of CRC incidence proportion trend and the change in percentage of CRC to all malignancies in male, female and in both over 20 years from 2000-2019.

Dependent variable (IP and %)	Independent variable	Constant b0	Coefficient b1	Standard error	95% CI	P value
All IP	Years	1.56	0.160	0.6211	4.4 - 10.07	<.001
Male IP	Years	1.83	0.156	0.6138	4.2 - 9.84	<.001
Female IP	Years	1.34	0.158	0.5469	4.7 - 10.30	<.001
Both %	Years	4.35	0.190	0.2094	-2.11 - 2.31	<.001
Male %	Years	4.59	0.208	0.1847	-2.45 - 1.98	<.001
Female %	Years	4.06	0.177	0.2747	-1.74 - 2.68	<.001

analysis outcome is shown in **Table 3**. The incidence significantly increased over the period 2000-2019 in all the age groups, but more significantly among adults aged 40–49 years. The minimum increase was seen in the age group 20-29 years

Sex-specific mortality proportion (SSMP) of CRC over 20-year period

The crude mortality proportion (CMP) per 100000

population increased slightly from 1.25 in 2010 to 1.77 per 100 000 population in 2019 (APC=4.1%). There was 4% annual increase in the male and female combined mortality proportion over the ten years period, but females had a lower mortality proportion than males (**Figure 3A, Table 4**). In males, there was a marginal but not statistically significant increase in SSMP from 1.41 in 2000 to 1.94 per 100 000 population in 2019 (APC=3.8%). Females had SSMP of 1.12 and 1.59 per

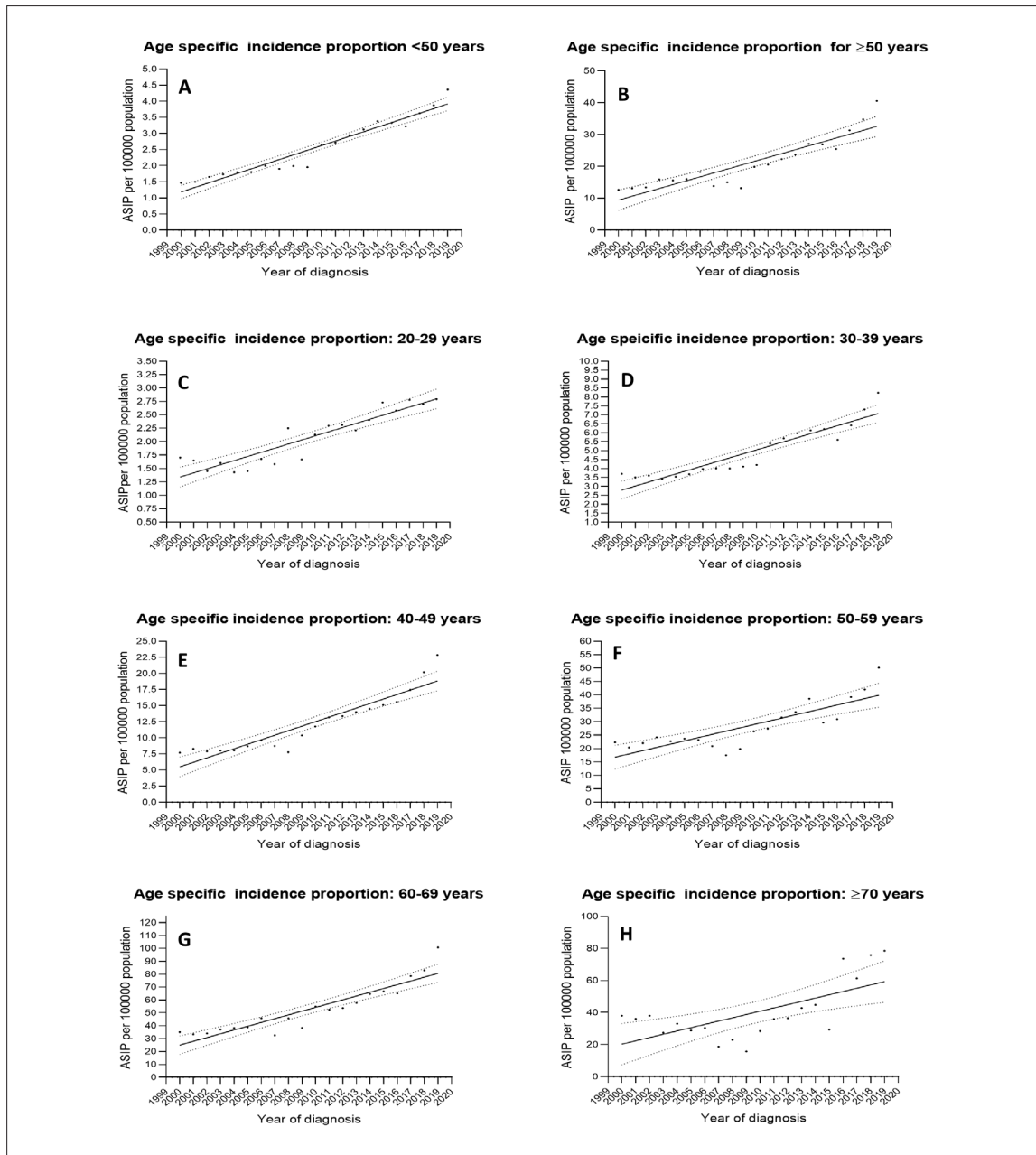


Figure 2. The age-specific incidence proportion of colorectal cancer over the 20-year period. The graphs A and B show the incidence of CRC in two age groups <50 and 50 years and older respectively. The incidence rate is higher in the latter group with similar average annual percentage increases. Graphs C to H are for the remaining ten year age groups. The peak of the disease was at 60-69 years; the lowest was for the age group 20-29 years.

Table 3. The results of linear regression statistical analysis of CRC age-specific incidence proportion (ASIP) trend over 20 years from 2000-2019 for males and females.

Dependent variable (age group)	Independent variable	Constant b0	Coefficient b1	Standard error	95% CI	P value
20-29	Years	1.26	0.0767	0.2025	5.7 - 11.21	<.001
30-39	Years	2.57	0.570	0.5482	2.7 - 8.40	<.001
40-49	Years	4.79	0.702	1.686	-5.0 - 1.7	<.001
50-59	Years	15.6	1.21	4.920	-22.6 - -13.1	<.001
60-69	Years	22.1	2.93	7.829	-51.5 - -33.1	<.001
>70	Years	18.2	2.05	14.25	-38.3 - -20.3	<.002
<50	Years	1.04	0.144	0.2311	5.2 - 10.75	<.001
>50	Years	8.23	1.22	3.510	-15.0 - -6.0	<.001

100000 population in 2000 and 2019 respectively, but not a statistically significant increase (APC=4.2%) (Figure 3A, Table 4). The CMP of CRC relative to all other cancers together rose from 4.4% in 2010 to 6.3% in 2019 (P<.001, APC=4.3%) (Figure 3B, Table 4). CRC was the eighth common cause of cancer deaths in 2000 and CRC became the fourth in 2019. The mortality rate has declined dramatically relative to incidence rate (Figure 3C).

CRC topography over 20 years

Colon (C18) was the most common CRC site in 2000 (59.2%), which rose in 2019 (65.7%) (P=.68, APC=0.5%). Lesions in the rectum (C20) were present in 37.2% of cases in 2000 decreasing to 31.4 in 2019 (P=.200, APC= 0.8%). Rectosigmoid junction (C19) tumors were seen in 3.6% in 2000 dropping to 2.9% in 2019 (P=.002, APC=0.9%). Sex-specific patterns were similar to findings for both sexes (Figure 4, Table 5).

CRC morphology trend over 20 years

The vast majority of the CRC cases in 2000 and 2019 were of adenocarcinoma histological type which increased significantly over 20 years (Table 6). Adenocarcinoma was the most common type. Other types such as epithelial, mucinous and carcinoid tumors were reported but none exceeded 5%. Other minor types such as epithelial tumour, mucinous adenocarcinoma and carcinoid tumor were reported over the 20-year period. There was a significant increase in adenocarcinomas and a reduction in the epithelial tumors (P<.001) (Table 7).

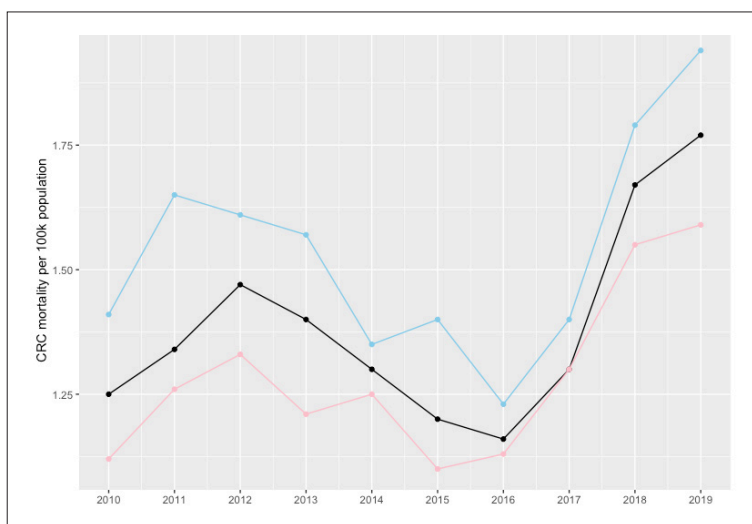


Figure 3A. Sex-specific mortality proportion of CRC cancer cases per 100000 population.

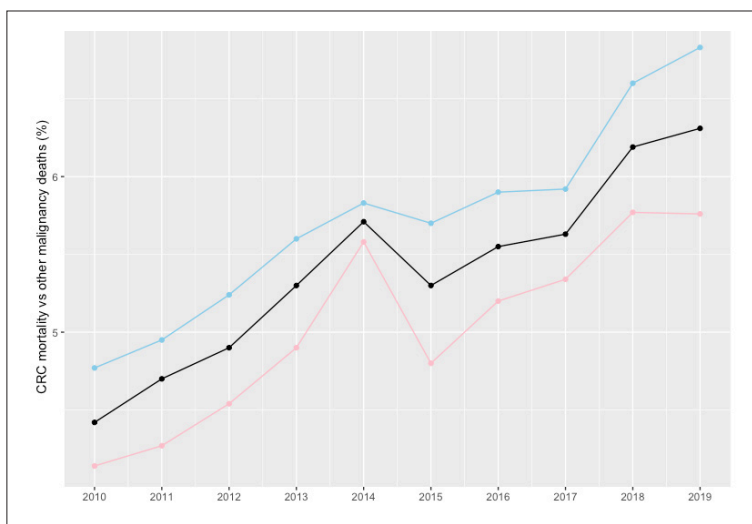


Figure 3B. CRC mortality in males and females relative to all cancer deaths over time. (Both sexes=black, Male=blue, Female=pink).

Table 4. Statistical analysis of CRC mortality proportion (MP) trend and the change in percentage (%) of CRC mortality to all malignancies deaths in males, females and in both over 10 years from 2010-2019. We also calculated the change in the mortality proportion to incidence proportion (MP to IP) over the same period.

Dependent variable (MP and %, CMP to CIP)	Independent variable	Constant b0	Coefficient b1	Standard error	95% CI	P value
MP both sexes	Years	1.21	0.0322	0.1839	1.94 - 6.285	.150
Male MP	Years	1.41	0.0226	0.2197	1.79 - 6.136	.377
Female MP	Years	1.09	0.0347	0.1411	2.05 - 6.385	.056
% both sexes	Years	4.35	0.190	0.2094	-2.11 - 2.31	<.001
Male %	Years	4.59	0.208	0.1847	-2.45 - 1.98	<.001
Female %	Years	4.06	0.177	0.2747	-1.74 - 2.68	<.001
MP both sexes to IP	Years	0.436	0.0167	0.0327	2.99 - 7.32	.0004
Male MP to IP	Years	0.469	0.0188	0.0411	2.97- 7.30	.0030
Female MP to IP	Years	0.433	0.0164	0.0259	2.99 - 7.32	.0004

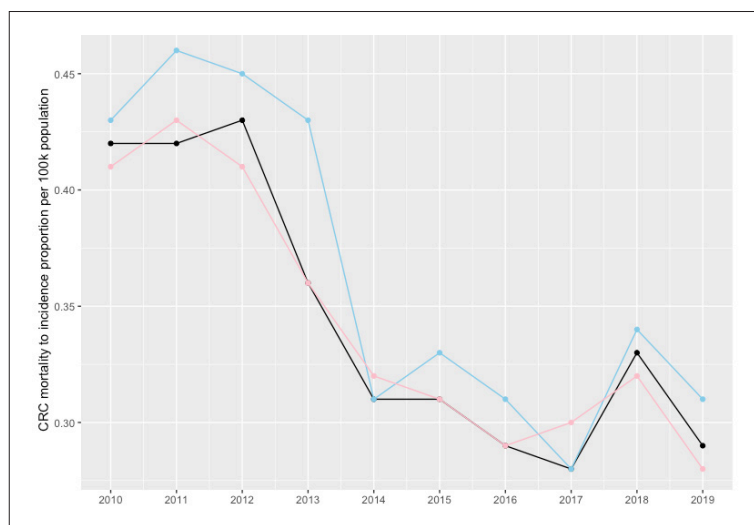


Figure 3C. The ratio of mortality proportion to incidence proportion per 100,000 population of CRC annually over ten years.

DISCUSSION

Colorectal cancer is a common malignancy that has been traditionally been seen as the disease of the elderly population of the Western world. However, as part of globalization, industrialization and urbanization, the trend is shifting toward a higher incidence of these diseases in the developing parts of the world.¹⁸ Luckily, Iraq is one of the countries that has a low incidence of CRC (<6.12/100,000 population) but it has been growing progressively over the last twenty years, in this work we determined the incidence by proportion not incidence, while other studies use incidence rate (IR) (both reflect the same meaning). Countries such as Australia

and some Northern European countries have a high IR (>32/100,000 population).⁵ Neighbouring countries such as Turkey, Iran, Saudi Arabia and Jordan have a relatively higher incidence rate of 24, 12, 10.5 and 9 per 100,000 population, respectively, according to recent statistics.^{4,19-21} Although the Iraqi CRC incidence figures are still relatively optimistic, the overall picture is gloomy. Theoretically, if the IP increase continues at this pace, the prediction is that Iraq would reach the Western IP by 2060.

The differences in the IR among countries is related to dietary, social and working life styles. Iraq has seen, over the last 18 years, a great economic transition from a country under embargo to a wealthy open economy, which has transformed all life aspects of the Iraqis toward the western lifestyle. Indeed, Iraq has seen increased consumption of alcohol and smoking, especially in the form of the Shisha pipe since 2003.²² There is a belief that ranges from rumour to partially science based that CRC is rising more in the young adult population. In our work, we found that there is a similar increase in the incidence proportion of CRC in those below 50 years of age and in those above 50 years. Our young adult incidence proportion is comparable to India and Iran and much lower than figures reported in the Western world such as Australia and the USA.^{23,24} The USA has witnessed a rise in the CRC incidence of about 25% in young adults over 13 years with a reduction of incidence in older adults. A similar pattern has been seen in Canada and Norway.¹³ Etiologically, ageing initiates the formation of cancers and provides milieu by enhancement of cancer driving mutations,²⁵ disruption of tissue structure and increased secretion

of degradative enzymes, inflammatory cytokines and growth factors by senescent cells.²⁶ In the recent years, it seems that these processes have begun earlier and the effect on cancer initiation and promotion appears earlier.

The male predominance in CRC in our work is a global trend; for example, British and Turkish statistics have shown a similar pattern.^{27,28} This gender variation might be related to sex-specific differences in the biological responses to dietary components.²⁹ The global mortality rate of CRC per 100000 population in both sexes was 8.9 in 2018, which is dramatically higher than the Iraqi figure of the same year (1.67) which might be due to low CRC IP in Iraq.³ In Iraq, all cancer mortality rates have seen a slight promising reduction over the last ten years while the CRC mortality rate increased significantly over the same period and consequently the share of CRC mortality relative to other malignancies almost doubled. In this study, there was a progressive reduction in the ratio of mortality proportion to incidence proportion over ten years (2010 to 2019). Possibly progress in the management of CRC has been made or the tumors are detected early; both would increase survival. The relative stability of the turbulent regions in Iraq after 2008 might have increased cancer registration and consequently incidence and mortality rates. As in other studies, the colon was the main site for the primary CRC tumor followed by the rectum.^{7,30} The Iraqi cancer registry did not detailed the colonic tumor topography as described by International Classification of Disease for Oncology (C18.0-C18.7).¹⁶

Our study would have been better if its span was longer and if it had included data about stages, grades and molecular characteristics to reveal more accurate trends of a disease like CRC that takes time to develop. Iraq has been in a state of war, instability and conflict over the last four decades which might have had an adverse effect on the registration process and the quality and quantity of the registered data. To conclude, there is a progressive increase in CRC incidence and fatality. This prevalence should be addressed by health authorities to redesign the screening program and to deal with patients with CRC more stringently. Governmental and non-governmental organizations should increase public awareness regarding CRC signs and symptoms and their potential risk factors.

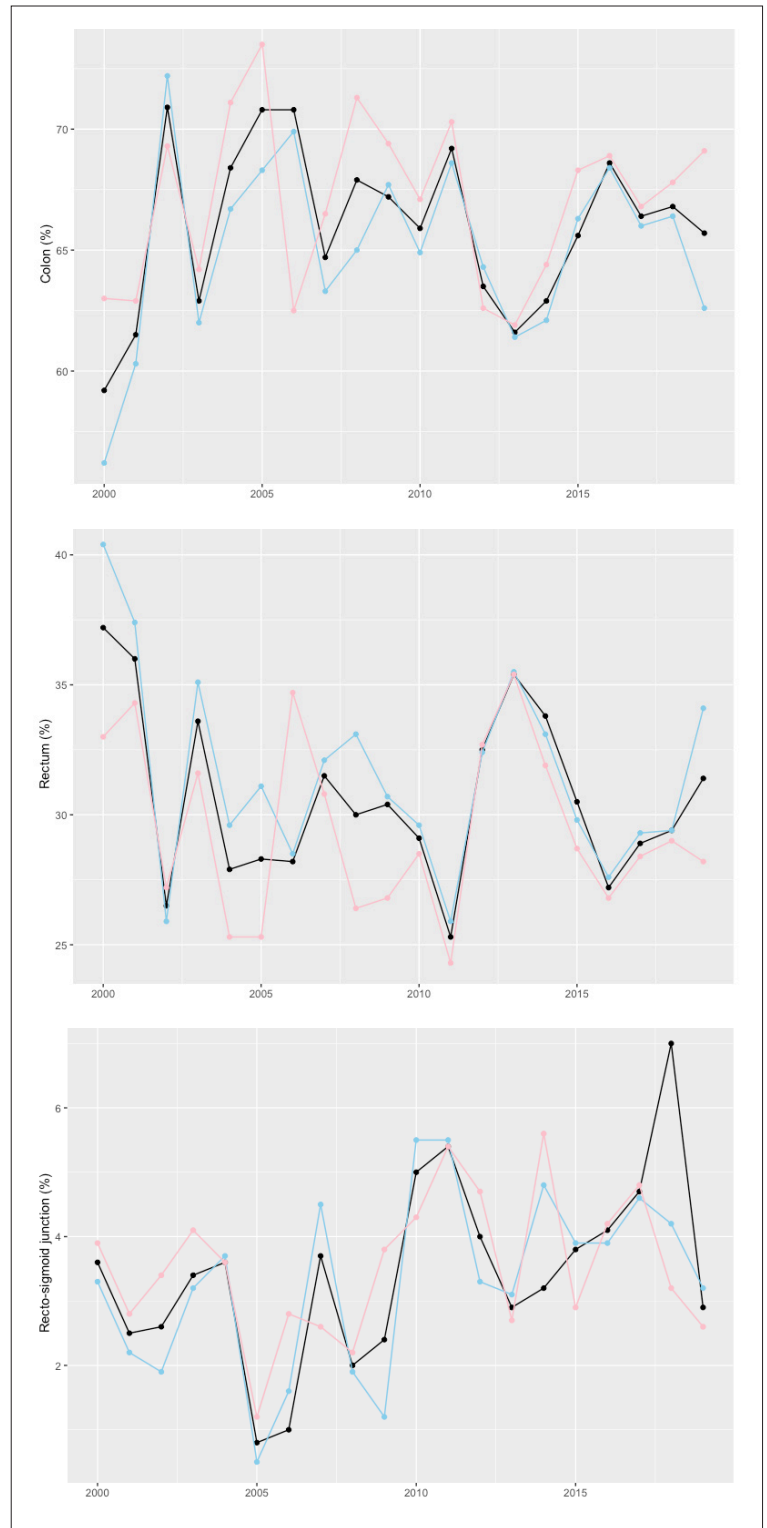


Figure 4. Percentages of specific anatomical CRC cases relative to other CRC cases.

Table 5. Statistical analysis of sex-specific differences in anatomic location of CRC (colon, rectum and colorectal junction) from 2020-2019.

Dependent variable (anatomic site)	Independent variable	Constant b0	Coefficient b1	Standard Error	95% CI	P value
Colon (both)	Years	65.6	0.0380	3.382	-57.65 - -53.40	.680
Rectum (both)	Years	31.9	-0.114	3.188	-56.81 - -52.45	.200
Colorectal junction (both)	Years	2.20	0.117	1.273	5.15 - 8.99	.002
Colon (males)	Years	64.3	0.082	3.803	-57.8 - -51.44	.586
Rectum (males)	Years	33.5	-0.191	3.640	-24.2 - -17.84	.193
Rectosigmoid junction (males)	Years	2.18	0.107	1.246	5.29 - 9.11	.003
Colon (females)	Years	66.4	0.0610	3.408	-58.68 - -54.41	.518
Rectum (females)	Years	30.4	0.0395	3.328	-21.09 - -16.84	.333
Rectosigmoid junction (females)	Years	3.10	0.0423	1.085	-23.21 - -18.85	.164

Table 6. Changes in frequency of histological types of CRC over 20-year period (separate data regarding each primary site histopathological type are not available in the INCR annual reports).

Year	Adenocarcinoma (%)	Epithelial tumor (%)	Mucinous adenocarcinoma (%)	Carcinoid tumors (%)	No report and other types (%)
2000	85.3	4.81	1.92	1.6	6.37
2001	77.89	3.86	1.8	1.8	14.65
2002	72.97	2.2	3.93	0	20.9
2003	77.96	0.65	3.56	0.32	17.51
2004	76.88	5.13	0.93	0.47	16.59
2005	87	5.1	1.5	0	6.4
2006	83	2.6	3.1	0.22	11.08
2007	81.8	3	3.5	0.83	10.87
2008	89	2	1.56	0.75	6.69
2009	89	4	2.6	0.14	4.26
2010	79	1	3.2	0.6	16.2
2011	73	1.4	3.09	0.67	21.84
2012	78	1.3	4.3	0.43	15.97
2013	81	2	3.9	0.45	12.65
2014	73	2.3	0.33	0.57	23.8
2015	93	0	3.6	0.3	3.1
2016	93.25	1.57	2.83	0.2	2.15
2017	84	0	4.8	0.46	10.74
2018	88.12	0	2.8	0	9.08
2019	90	0	3.54	0	6.46

Table 7. The results of statistical analysis of CRC histological types percentage over 20 years from 2020-2019 in males and females (crudes), here we selected five histological types only since other types have very small contribution.

Dependent variable (histological type)	Independent variable	Constant b0	Coefficient b1	Standard error	95% CI	P value
Adenocarcinoma	Years	78	0.442	6.139	-76.1 – 68.2	<.001
Epithelial tumors	Years	4.33	-0.208	1.220	5.5 – 11.21	<.001
Mucinous tumors	Years	2.16	0.064	1.136	4.8 – 10.47	.164
Carcinoid tumors	Years	0.906	-0.0395	0.438	7.2 – 12.79	.032
Other types or no reports	Years	14.6	-0.258	6.383	-5.3 – 2.6	.311

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