

Pattern of Colorectal Cancer in Karbala Province of Iraq: Data from Developing Country

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Background: Globally, there are differences in the prevalence of colorectal cancer (CRC) depending on environmental and demographic factors.

Objective: Our study's objective was to analyze the CRC pattern in the Iraqi province of Karbala, comparing and identifying probable variations with another people.

Methods: In Iraq, at the Al-Hussein Cancer Center in Karbala, retrospective descriptive research was conducted on 524 patients who diagnosed with CRC from January 2012 to December 2020.

Results: The incidence rate of CRC increased from 3.83 per 100,000 in 2012 to 5.69 per 100,000 in 2020. Among our patients, median age was 55 years. The proportion of males was (54.96%) while the proportion of females was (45.04%) with a M:F ratio of (1.22:1). The most affected anatomical site was colon in (64.89%) and adenocarcinoma was the most frequent histopathology in (67.18%). Unfortunately, more than 46% of cases presented as stage III & IV.

Conclusion: This statistical analysis of CRC could be a fundamental knowledge source to analyze epidemiological pattern, to assess development in the last few years and to improve treatment plans.

Introduction

Colorectal cancer (CRC) ranks third globally in terms of mortality and fourth in terms of frequency of diagnosis, according to GLOBOCAN 2018 data [1]. There is huge variation in CRC incidence between developing and developed countries. In Iraq, CRC represents 6% of registered cancer cases [2]. The low incidence in developing countries will change in future due to adaptation of western life style and nutritional habits [3]. Family history and first-degree relative with CRC are associated with high risk. While obesity, sedentary life style, smoking, low vegetables and fruits consumption, increase red meat eating are related to moderate risk [4]. The differences in exposure to those risk factors may lead to huge difference in cancer incidence from country to other [5]. There is limited information available regarding the CRC pattern in Iraq, and the majority of the statistics come from industrialized nations.

In this research we will evaluate the epidemiological pattern of CRC in the Iraqi province of

Karbala between 2012 and 2020. This research could give basic data to investigate the epidemiological aspects of CRC, assessing recent advances, and developing future treatment plans.

Materials and Methods

Study design and participants

Retrospective descriptive study on CRC patients diagnosed between January 2012 and December 2020 was conducted at Al-Hussein Cancer Center in the Iraqi province of Karbala. During that period 524 patients were diagnosed with CRC. In addition to treating the people of Karbala, patients are sent to our institution from the Middle Euphrates Region of Iraq for the management of hematological and solid malignancies [6, 7]. Patients were diagnosed by colonoscopy and samples were sent to pathological department for final diagnosis. Rectal cancer was regarded in location within 12 cm from anal verge [8]. Staging of patients was either by CT scan or by PET scan if available. Collected data also provided information about age, sex, residence, year of diagnosis, history of inflammatory bowel disease, family history of CRC and smoking.

Inclusion / Exclusion criteria

All patients with CRC diagnosed between January 2012 and December 2020 were included in this research. Patients whose results were not conclusive were not included in the research.

Ethical considerations

The Ethics Committee at the Karbala Teaching Hospital in Karbala, Iraq, provided ethical approval.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) software (version 25) was used to enter and manage patients' data. The variables' descriptive statistics were presented as a number, median, percentage and range.

Results

Incidence

In period between 2012-2020, 524 cases with CRC were registered in our institution. The overall incidence rate was increased from 3.83 per 100,000 in 2012 to

5.69 per 100,000 in 2020. For males the incidence rate increased from 4.20 per 100,000 in 2012 to 6.33 per 100,000 in 2020. While for females the incidence rate increased from 3.44 per 100,000 in 2012 to 5.03 per 100,000 in 2020. The percentage of CRC cases out of all diagnosed cancers ranged between 8.69% in 2012 and 5.47 % in 2020 as shown in (Figure 1, Table 1 and 2).

Figure 1. Percentage of CRC Out of all Cancers 2012-2020.

| Year | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|-----------|------|------|------|------|------|------|------|------|------|
| All cases | 3.83 | 2.49 | 3.04 | 4.49 | 5.45 | 6.65 | 5.49 | 6.47 | 5.69 |
| Males | 4.2 | 2.61 | 2.99 | 4.2 | 5.89 | 8.51 | 6.18 | 6.5 | 6.33 |
| Females | 3.44 | 2.39 | 3.07 | 4.79 | 5 | 4.76 | 4.8 | 6.45 | 5.03 |

Table 1. Incidence Rates of CRC per 100,000 in Karbala, 2012-2020.

| Year | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Colorectal cancer | 42 | 28 | 35 | 53 | 66 | 79 | 67 | 81 | 73 |
| All Cancers | 483 | 555 | 655 | 861 | 1043 | 1213 | 1164 | 1256 | 1333 |
| Percentage | 8.69% | 5.04% | 5.34% | 6.15% | 6.32% | 6.51% | 5.75% | 6.44% | 5.47% |

Table 2. Number of New Cases of CRC and All Cancers Per Year.

Sex distribution

Among our patients an apparent male predominance was seen, as 288 patients (54.96%) were males and 236 patients (45.04%) were females, with a M:F ratio 1.22:1 as shown in (Figure 2).

Figure 2. Distribution of CRC Cases by Gender 2012-2020.

Age distribution

Median age was 55 years, range (16-95) years. The most frequent age group was (61-70) years in 139 patients (26.53%) followed by (51-60) years in 108 patients (20.61%) and (41-50) in 107 patients (20.42%) as shown in (Table 3).

| Age (year) | N (%) |
|------------|-------------|
| ≤ 20 | 6 (1.14) |
| 21-30 | 39 (7.44) |
| 31- 40 | 65 (12.40) |
| 41-50 | 107 (20.42) |
| 51-60 | 108 (20.61) |
| 61-70 | 139 (26.53) |
| 71-80 | 47 (8.97) |
| 81-90 | 10 (1.91) |
| >90 | 3 (0.57) |

Table 3. Age Distribution of 524 Patients.

Geographic distribution and risk factors

About 340 patients (64.89%) lived in urban areas and 184 patients (35.11%) lived in rural areas. Thirty-five patients (6.68%) had family history of CRC; 20 patients (3.82%) diagnosed previously with inflammatory bowel disease. Seventy-four patients (14.12%) were smokers, 115 patients (21.95%) were ex-smokers and 335 patients (63.93%) were nonsmokers as shown in (Table 4).

| Variables | Number (%) |
|----------------|-------------|
| Residence | |
| Urban | 340 (64.89) |
| Rural | 184 (35.11) |
| Family history | |

| | |
|----------------------------|-------------|
| Yes | 35 (6.68) |
| No | 489 (93.32) |
| Inflammatory bowel disease | |
| Yes | 20 (3.82) |
| No | 504 (96.18) |
| Smoking | |
| Smoker | 74 (14.12) |
| Non- smoker | 335 (63.93) |
| Ex-smoker | 115 (21.95) |

Table 4. Geographic Distribution and Risk Factors of 524 Patients.

Sites of tumors

There were 340 patients (64.89%) diagnosed as colonic tumor, 148 patients (28.24%) as rectal tumor and 36 patients (6.87%) as rectosigmoid tumor as shown in (Figure 3).

Figure 3. Sites of Tumors.

Pathological subtypes

Regarding the pathological subtypes, adenocarcinoma was the most frequent subtype in 352 patients (67.18%) followed by mucinous type in 62 patients (11.83%), undifferentiated type in 36 patients (6.87%), signet ring in 20 patients (3.82%), neuroendocrine in 11 patients (2.10%), adeno-squamous in 11 patients (2.10%%), lymphoma in 6 patients (1.14%) and other pathological subtypes in 26 patients (4.96%) as shown in (Figure 4).

Figure 4. Pathological Subtypes of CRC.

Stages of cancer

Regarding the stage of disease, the most common stage was stage IV in 127 patients (24.24%), followed by stage II in 120 patients (22.90%), stage III in 116 patients (22.14%), stage I in 57 patients (10.88%) and stage 0 in 10 patients (1.90%). While 94 patients (17.94%) were unknown stage as shown in (Figure 5).

Figure 5. Stages of 524 Patients at Time of Diagnosis.

Discussion

It is assumed that the prevalence of CRC in Iraq would continue to rise in the future. The contributing factors to the rising prevalence of CRC in Iraq are alterations in lifestyle & eating habits (Western food poor in fiber and heavy in fat), inactivity, and sedentary behavior among Iraqi people [9, 10].

Overall, there are significant regional differences in CRC incidence, often varying by up to eight times between the nations. Incidence rates typically increase in nations that are going through significant developmental transitions [11]. The incidence rate in Karbala was increased from 3.83 per 100,000 in 2012 to 5.69 per 100,000 in 2020. Our results were close to South-Central Asia (5.5

per 100,000) and Western Africa (6.7 per 100,000). On the other hand, our findings much lower than Northern Europe (33.6 per 100,000) and Northern America (26.2 per 100,000). These variations may be explained by variation in lifestyle and exposure to risk factors [11, 12].

Interestingly, the percentage of CRC out of all diagnosed cancers ranged between 8.69% in 2012 and 5.47 % in 2020. This decline in percentage can be explained by improving in registration system of various cancer types in our province [13].

As the previous international studies, CRC in our province affected males more than females. Males' mortality rates from CRC are much greater than females' mortality rates, indicating that sex and gender play a key role in the illness [14].

The majority of CRC patients in this study were between the ages of 50 and 70 years, which is in line with findings from other previous studies conducted in Iraq, Jordan and Iran [15-17]. Interestingly, about 40% of our patients were ≤ 50 years this may be because of high percent of Iraqi population were young age groups ($> 58\%$ of population under 25 years old) [18].

The differences in CRC survival between urban and rural areas are unclear, and the potential prognostic factors for CRC survival in urban and rural areas are unclear [19]. In our province more than 60% of cases lived in urban area. This may be due to the urban transformation of Karbala population in the last decades [20]. Patients with family history of CRC represent about 6.68% of our cases. In fact, family history is one of established risk factor for CRC, which includes both genetic and shared environmental hazards. It might still be an effective clinical tool for determining who is more likely to develop CRC [21].

Crohn's disease and ulcerative colitis are the two main disorders of inflammatory bowel disease. Compared to the general population, people with inflammatory bowel disease colitis have a six-fold increased risk of developing CRC [22]. Our results revealed that only 3.82% of our patients had inflammatory bowel disease which was close to what observed in previous international percentage with about 3% [22].

The link between CRC and cigarette smoking has shown inconsistency between researches, about 36% of our patients were exposed to tobacco. But due to the influence of additional confounding factors, neither the International Agency for Research on Cancer (IARC) nor the U.S. Surgeon General have identified this link as causative [23].

In our study, the most affected site was colon in 64.89% followed by rectum in 28.24% and rectosigmoid in 6.87%. These results were close to what recorded in Iran where 61.83% of patients were colon cancer, 27.54 % were rectal cancer and 7.46 % were rectosigmoid cancer [24]. Same results in United States where more than 66 % of the anatomical location of the CRC was the colon [25]. However, the growing use of diagnostic methods like colorectaloscopy is contributing to an increase in proximal colon cases [24].

In term of histopathology, the most common type was adenocarcinoma which is consistent with previous studies in Iran and Japan [24, 26]. The percentage of patients presenting with advance stage is high in Iraq, more than 46% of cases presented as stage III & IV. Same results in Saudia Arabia and India where the CRC diagnosed at late stages [27, 28]. On the other hand, only 20% of patients in the United States have distant metastatic disease at the time of presentation [28]. This delay in the diagnosis may be due to lack of awareness about cancer in Iraq, which is an important barrier for early diagnosis and management of cancer patients [29].

Our research might be assessed in regarding of its strengths and limitations. Our study's ability to offer basic information regarding CRC in Iraq and compare it to surrounding countries and the rest of the world is one of its strengths. On the other hand, exclusive focus on the Karbala area and exclusion of other regions of Iraq is one of our research's limitations.

In conclusion, in Iraq, the incidence of CRC is increasing. This has a major burden on national health system in our county. Insufficient screening programs and education efforts about CRC symptoms are the reason for the higher percentage of advanced stage cancer at presentation when compared to developed nations. Our research emphasizes the necessity of additional researches in further regions of the country with more patients to identify the CRC distribution and pattern in Iraq.

Acknowledgments

Statement of Transparency and Principals:

- Author declares no conflict of interest
- Study was approved by Research Ethic Committee of author affiliated Institute.
- Study's data is available upon a reasonable request.
- All authors have contributed to implementation of this research.

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