Short Communications

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Colorectal Cancer in Saudi Arabia: The Way Forward

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Abstract

Colorectal cancer is the most common cancer in Saudi males and the second most common cancer in Saudi females with increasing incidence throughout the last four decades. Although the disease incidence is on the rise, still there is no systemic screening for colorectal cancer in the Saudi population. Early onset colorectal cancer is common in the Saudi population and up to 50% in Saudi patients diagnosed at late stages with regional and distal metastasis. Therefore, more efforts are required to control the disease in the Kingdom of Saudi Arabia. In this regard, systematic work at national level is highly required to make colorectal cancer screening for population at risk part of the routine primary health care activities. This paper highlights the current situation of colorectal cancer in the Kingdom of Saudi Arabia with relation to incidence, mortality and morbidity in addition to the disease control efforts going on. Finally, some recommendations are provided to strengthen the control program of colorectal cancer.

Keywords: Colorectal carcinoma- colorectal neoplasm- cancer control- colon cancer- rectal cancer

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Introduction

Worldwide, Colorectal cancer (CRC) ranks the third in term of incidence, with approximately 1.9 million new cases (10%), but the second in term of mortality with approximately 935,000 deaths (9.4%) in 2020 (Sung et al., 2021). The incidence rates of CRC show a wide geographical variation, with the highest rates in Southern Europe (ASR 39.9 and 23.7 per 100,000 for males and females respectively), Northern Europe (ASR 38.3 and 27.2 per 100,000 for males and females respectively), Australia/New Zealand (ASR 36.4 and 27.7 per 100,000 for males and females respectively). The incidence of CRC tends to be low in most regions of Western Africa (ASR 7.0 and 5.1 per 100,000 for males and females respectively), and in South Central Asia (ASR 6.2 and 4.0 per 100,000 for males and females respectively) (Sung et al., 2021). In general, the incidence of CRC in high/very high Human Development Index (HDI) countries is higher (ASR 29.0 and 7.4 per 100,000 for males and females respectively) than in the low- and middle HDI countries (ASR 20.0 and 5.4 per 100,000 for males and females respectively) (Sung et al., 2021; Arnold et al., 2020).

According to Saudi cancer incidence report in 2018, CRC is the most common cancer among men (15.3%) and third among women (9.8%) (Table 1). Despite the high incidence of CRC in the Kingdome of Saudi Araba (KSA) (Makhlouf et al., 2021), there is a paucity of data reporting the burden of CRC in this region. This work highlights the current situation of CRC in KSA with relation to incidence and mortality in addition to the disease control efforts going on.

Colorectal cancer is on the rise in Gulf Cooperation Council States

Gulf Cooperation Council (GCC) states include KSA, Kuwait, Qatar, Bahrain, United Arab Emirates (UAE) and Sultanate of Oman. The population of GCC in 2020 was approximately 57.6 million, of whom 49% are expatriates (GCC-STAT, 2022; Khoja et al., 2017). The GCC populations are young, with about half of the population is currently under age 30 years old. Improvements in health care services have led to an increase in life expectancy from 62 years in 1970 to surpasses 77 years in the last decade. By the year 2040, the predicted numbers of newly diagnosed cancers and cancer deaths in the older population will increase by 465% and 462% respectively in GCC due to demographic changes (Cheema et al., 2021). This region has also witnessed changes in diet and lifestyle pattern. Moreover, the obesity rate in this region is one of the highest in the world (Khoja et al., 2017). These changes might also have affected the incidence

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and pattern of cancer in these countries. In this regard, the leading cause of death from infectious diseases in this region was replaced with a predominance of chronic diseases, including cancer.

In GCC states, CRC is the second most common type of cancer. Over all, the highest estimated ASR of CRC across all ages in GCC was reported in Qatar (15.9 per 100 000), while the lowest rate was reported in Oman (9.9 per 100 000). Among male population, the highest and lowest ASR were reported in KSA (16.1 per 100,000) and Oman (11.2 per 100,000), respectively. The highest ASR among female was reported in Qatar (20.6 per 100,000), followed by UAE (17.3 per 100,000) and Bahrain (14.6 per 100,000) as shown in Table 2. (Arnold et al., 2019). The percentage of patients presenting with regional and/or distant metastasis is high (Alsanea et al., 2015; Dehni et al.,2012; Kumar et al., 2015). Notably, recent advances in early detection screenings and treatment options have reduced CRC mortality in Europe and North America. However, the 5-year survival in GCC is still suboptimal due to lack of national screening programs and a higher proportion of advanced stage cancer at presentation (Sung et al., 2021; Alsanea et al., 2015).

Colorectal cancer is on the rise in Kingdom of Saudi Arabia

KSA is a high-income country located in Western Asia on the Arabian Peninsula. It has a land area of about 2,150,000 km², making it the fifth-largest country in Asia, the second-largest in the Arab world. The current population of KSA is approximately 36 million persons, making it the most populous country among the GCC countries (https://www.worldometers.info), (https://worldpopulationreview.com).

The incidence of cancer in KSA is increasing continuously over the last decades. In 2020, the total number of all cancer cases was 27885 with 4007 CRC cases representing 14.4% of all diagnosed cancers in both sexes. The most common malignancies among the overall Saudi population are breast cancer, CRC, and thyroid cancer (https://gco.iarc.fr/today/data/factsheets/populations/682-saudi-arabia-fact-sheets.pdf).

Incidence of CRC in KSA

CRC is the second most common cancer among Saudi population. It is the most common cancer in Saudi males with ASR 13.9 per 100,000 followed by non-Hodgkin's lymphoma with ASR 6.3 per 100,000 and prostate cancer with ASR 7.2 per 100,000. In Saudi females, CRC is the third most common cancer with ASR 11.3 per 100,000 preceded by breast cancer with ASR 33.7 per 100,000 and thyroid cancer with ASR of 13.7 per 100,000 (Table 1). The incidence of CRC among Saudi population seems to be increasing continuously over the last decades (Chaudhri et al., 2020). The reports of the Saudi Cancer Registry (SCR), established in 1994, show this rise in the incidence of CRC in KSA (Ibrahim et al., 2008). In Saudi Arabia, male's ASR for CRC has increased from 9.9 in the year 2006 to 14.2 in the year 2018, while for females, ASR has increased from 8.8 in 2006 to 11.5 in the year 2018. Overall, the number of CRC cases diagnosed per year in Saudi Arabia have increased between 2002 and 2017 for males and females, but males consistently had higher ASR than females (Table 3 and Figure 1). The increasing incidence rate of CRC in Saudi Arabia may be attributed to increasing adoption of sedentary lifestyle with less physical activity (Alqahtani et al 2021), high obesity (BMI >30 kg/m²) rates (24.1% and 33.5% for males and females respectively) as well as high overweight (BMI 25-30 kg/m²) rates (33.4% and 28% for males and females respectively) in addition to other CRC risk factors such as low dietary fiber intake and high red meat intake (Nashar and Almurshed, 2008). There are no available comprehensive reports to elucidate the roles of environmental factors behind this increase in the incidence of CRC in Saudi Arabia with exception of few studies with small sample size (Nashar et al., 2008; Azzeh et al., 2017; Alazzeh et al., 2018).

Regional Distribution of CRC in Saudi Arabia

The cancer incidence report in Saudi Arabia for the

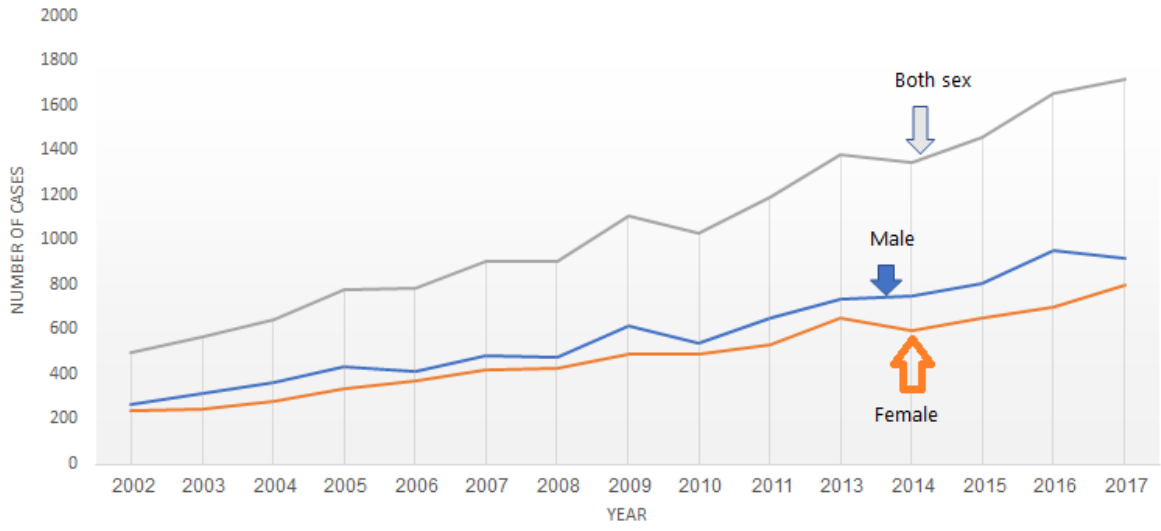

Figure 1. Colorectal Cancer Cases in Saudi Arabia. Information was Collected from the Saudi Cancer Registry https://nhic.gov.sa/en/eServices/Pages/TumorRegistration.aspx

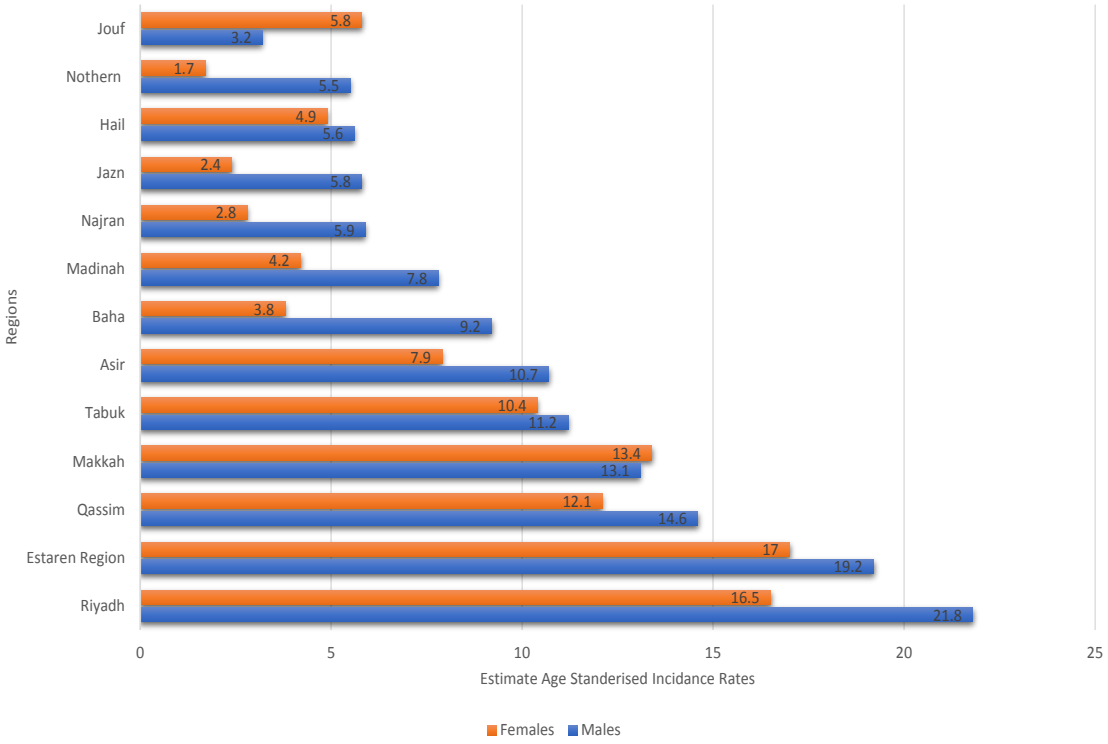

Figure 2. Regional Distribution of Colorectal Cancer in Saudi Arabia Shown by Estimated Age Standardized Incidence Rates per 100,000 Population. Source: Cancer Incidence Report in the Kingdome of Saudi Arabia 2018 by the Saudi Health Council (2022): ISBN: 978-603-04-2168-8

Table 1. Age Standardized Incidence Rate, Number of Cases and Percentages of the Most Common Cancers in Saudi Males and Females

	Number of cases	%	ASR
Males			
Site			
Colorectal	1045	15.3	13.9
Non Hodgkin's Lymphoma	552	8.1	6.3
Prostate	475	6.9	7.2
Leukemia	466	6.7	4.4
Bladder	388	5.7	5.3
Lung	349	5.1	5.0
Hodgkin's Lymphoma	337	4.9	3.1
Liver	332	4.8	4.8
Kidney	282	4.1	3.5
Thyroid	278	4.1	2.9
Females			
Site			
Breast	2814	31.8	33.7
Thyroid	1045	11.8	13.7
Colorectal	863	9.8	11.3
Corpus Uteri	564	6.4	7.9
Non Hodgkin's Lymphoma	371	4.2	4.5
Leukemia	333	3.8	3.7
Ovary	286	3.2	3.5
Hodgkin's Lymphoma	207	2.3	2.0
Brain, CNS	184	2.1	2.0
Cervix Uteri	176	2	2.2

year 2018 has indicated a marked regional variation in the incidence of CRC expressed in ASR as shown in Figure 2. Riyadh region reported the highest incidence with an ASR of 21.8 and 16.5 for males and females respectively, it was followed by the Eastern, Qassim and Makkah regions. Asir region was at middle with an ASR of 10.7 and 7.9 for males and females respectively. The lowest incidence for CRC was reported by Jouf region with an ASR of 3.2 and 5.8 for males and females respectively. This wide variation in the incidence of CRC among different regions of Saudi Arabia may be partially attributed the variation of CRC detection rates that may be due to variation in the availability of health services.

Table 2. Estimated Age Standardized Colorectal Cancer in 2020 Across All Ages in Gulf Cooperation Council States

Population Country	Both Sexes ASR	Male ASR	Female ASR
Qatar	15.7	13.6	20.6
KSA	13.9	16.1	10.9
Bahrain	13.9	13.7	14.6
UAE	13.1	11.5	17.3
Kuwait	12.5	13.1	11.9
Oman	9.9	11.2	7.7

Abbreviation: ASR, Estimated age standardized incidence rate per 100 000; KSA, Kingdome of Saudi Arabia; UAE, the United Arab Emirates Source: Arnold M et al (2019). ICBP SURVMARK-2 Online tools: International cancer Survival Benchmarking. Lyon, France: International Agency for research on Cancer. Available from: http://gco.iarc.fr/survival/survmark, accessed [17/June/2022]

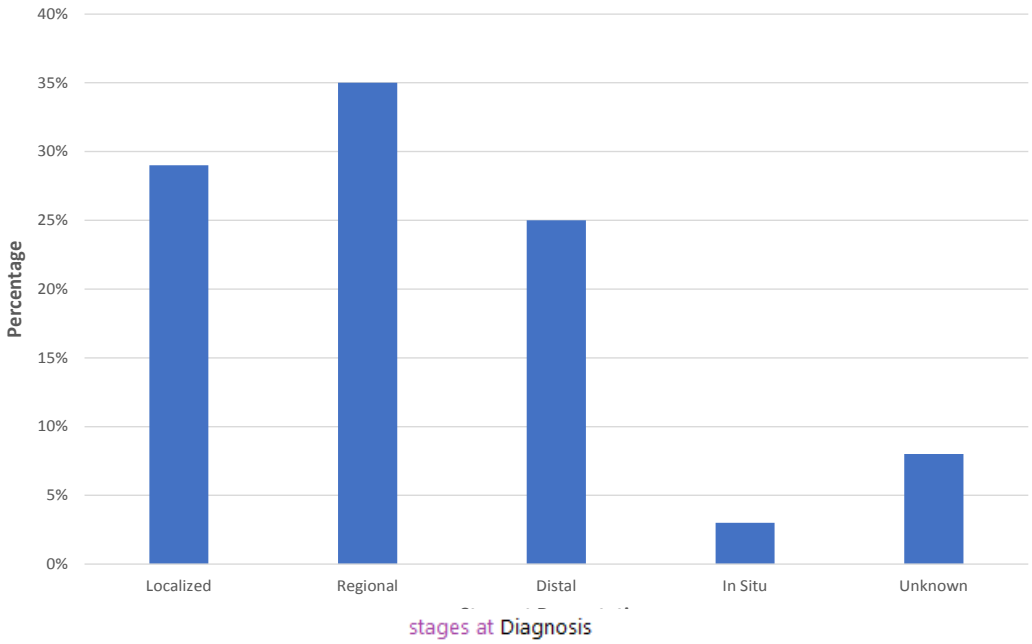

Figure 3. Stages Distributions of Colorectal Cancer among Saudi PatientsSource. Source: Cancer Incidence Report in the Kingdome of Saudi Arabia 2018 by the Saudi Health Council (2022): ISBN: 978-603-04-2168-8

Table 3. Number of New Colorectal Cancer Cases and Estimated Age Standardized Incidence Rates Per 100,000 Population among Saudi Males and Females (2006 and 2018)

Year	All cases	Male (%)	Female (%)	Male (ASR)	Female (ASR)
2006	784	53%	47%	9.9	8.8
2007	907	54%	46%	9.8	8.3
2008	904	53%	47%	9.1	8.3
2009	1109	56%	44%	12	9.7
2010	1033	52%	48%	10.2	9.4
2011	1194	55%	45%	11.5	9.3
2012	1230	55%	45%	11.5	9.2
2013	1387	53%	47%	11.8	10.2
2014	1347	56%	44%	11.1	8.4
2015	1465	55%	45%	11.4	9.2
2016	1659	58%	42%	13.2	9.7
2017	1720	53%	47%	12.8	11.1
2018	1881	44%	56%	14.2	11.5

Source: Saudi Cancer Registry Reports for the Years (2006-2018); https://shc.gov.sa/Arabia/NCC/Activities/pages/annualReorts.aspx

It would be an interesting research aim to illuminate the reasons behind this marked variation in the incidence of CRC in the different geographical regions of Saudi Arabia.

Epidemiological aspects of CRC in Saudi Arabia

Early onset CRC in common in the Saudi population. This could be due to the fact that over 85% of the Saudi population are younger than 50 years old, which put them at heightened risk of early-onset CRC. The median age at presentation of CRC in Saudi women and men were 55 years and 60 years, respectively (Al-Eid and Garcia, 2014). Despite a well-established healthcare system in KSA; diagnosis at late stages with regional and distal metastasis of up to 50% was observed in Saudi patients with CRC diagnosis (Figure 3). Insufficient Knowledge about CRC, a possible factor for late presentation, was reported among Saudi population (Alsulaim et al., 2021)

In young Saudi patients with CRC, the disease presents with more advanced stages and poorly differentiated tumors than in older patients (Al-Ahwal, Alghamdi, 2005). Adenocarcinoma is the most frequent histopathological type accounted to 79.5% of CRC in Saudi males and 82% in Saudi females (Table 4). The frequency of the Kristen Rat Sarcoma (KRAS) mutations (42.2%) in the Saudi population with CRC (Bader, and Ismail, 2014), appears to be comparable to the prevalence rates of KRAS (44.4%) mutations in Arab population (Al-Shamsi et al., 2016), but higher than the frequency reported (30% - 37%) in previous studies from western countries (Addreyev et al.; 1998; Smith et al., 2002). KRAS mutated CRC patients had a higher propensity for lung metastases by-passing liver metastases indicating the need for more extensive chest imaging for effective staging. Furthermore, patients with mutation in extended RAS family are resistant to anti EGFR medications such as cetuximab and panitumumab that used for treatment of RAS wild-type metastatic CRC.

Survival of CRC in Saudi Arabia

Data on survival of CRC in Saudi Arabia is limited. Previous studies reported 5-year survival rates among Saudi population between 44%-52% (Alsanea et al., 2015; Alyabsi et al., 2021), compared with more than 60% in the USA (Siegel et al., 2021). Stage for stage, the 5-year survival was 80% for localized stage, 63% for regional stage and 20% for distant metastasis (Alyabsi et al., 2021). These rates are lower than reported 5-year survival rates from USA which ranges from 90% for patients diagnosed with localized disease to 14% for those diagnosed with

Table 4. The Morphological Distribution of Colorectal Cancer among Saudi nationals in 2018

ICD Code	Morphology	Male		Female	
		n	%	n	%
81403	Adenocarcinoma, NOS	861	82.4	692	80.2
84803	Mucinous adenocarcinoma	63	6	66	7.6
82633	Adenocarcinoma in tubulovillous adenoma	19	1.8	21	2.4
80103	Carcinoma, NOS	15	1.4	16	1.9
84903	Signet ring cell carcinoma	13	1.2	9	1
80003	Neoplasm, malignant	11	1.1	9	1
82463	Neuroendocrine carcinoma, NOS	11	1.1	8	0.9
81443	Adenocarcinoma intestinal type	10	1	5	0.6
81443	Adenocarcinoma, adenomatous polyp	9	0.9	5	0.6
82613	Adenocarcinoma in villous adenoma	7	0.7	8	0.9
-	Others	26	2.5	24	2.8
Total		1045	100	836	100

Source, Saudi Health Council (2022); ISBN, 978-603-04-2168-8

distant-stage (Al-Ahwal et al., 2013; Siegel RL 2021). Despite a well-established healthcare system in KSA; diagnosis at late stages, driven by poor public awareness and lack of CRC screening as well as diagnostic pathways is associated with increased risk of death among Saudi patients with CRC (Al-Ahwal and Alghamdi, 2005; Alyabsi et al., 2021; Khayyat and Ibrahim, 2014; Alaqel et al., 2021).

Risk factors of CRC in Saudi Arabia

The global geographic variations in the incidence of CRC are thought to be multifactorial (Sung et al., 2021). Many risk factors have been studied and some proved to be associated with increased risk to the disease. These risk factors may differ from region to the other as many of the reported risk factors are related to lifestyle and eating habits. Hereditary factors play a definite role (Heavy et al., 2004) as approximately 13% of early-onset CRC develops from germline mutations in a known hereditary cancer gene (Daca Alvarezet al., 2021). Other risk factors include age over 50 years (Sial et al., 2001), Inflammatory bowel disease (Triantafillidis et al., 2009), a diet low in fiber and diets rich in red and processed meat (Baena and Salinas, 2015), physical inactivity (Wu et al., 1978), and obesity (Frezza et al., 2006), alcohol, tobacco, smoking and others (Wu et al., 1987; Botter et al., 2008). lifestyle factors such as physical inactivity, obesity, and tobacco smoking are major lifestyle factors that could be responsible of a huge fraction of CRC cases among both genders in Saudi Arabia (Nashar and Almurshed, 2008). Obesity is common among Saudi population, similar to other GCG. A nationwide cross-sectional survey conducted in 2020 by Althumiri et al., (2021) revealed that 24.7% of Saudi population are considered obese (BMI ≥ 30). According to WHO, more than one third of Saudi adults and one in five adolescents are considered obese (WHO, 2018). Obesity since early adulthood were associated with raise in early-onset CRC (Liu et al., 2019). With regard to smoking, data pooled from two national surveys conducted in 2018 across the 13 regions of KSA showed that the prevalence of cigarette smoking was 21.4% of the population. The prevalence of smoking was 32.5% among Saudi males and 3.9% among Saudi females (Algabbani et al., 2015). The drastic changes in the lifestyle and food consumption patterns such as westernizing diet, increased consumption of carbohydrates and sedentary lifestyle may also have affected the incidence of CRC in KSA.

Colorectal Cancer Early Detection in Saudi Arabia

The Colorectal Cancer Early Detection project in Saudi Arabia aims at early detection of CRC in citizens aged 50 years or older. Following are the objectives of the project:

1. Reduce the incidence of the disease.
2. Increase the success rate of treatment.
3. Reduce the colorectal cancer mortality rate.
4. Improve the quality of lifestyle of colorectal cancer patients.

The project uses a number of investigations for early detection of CRC such as fecal occult blood test (FOBT) and colonoscopy., When the FOBT result is negative, it will be repeated once a year, when the test is positive, the patient is referred for colonoscopy. When it is negative: colonoscopy is repeated: once every 5 years for people at moderate risk of the disease and once a year for those at high risk of the disease. When colonoscopy is positive, the patient will be referred for further investigations and therapy. Despite all these efforts still there is no countrywide screening program for CRC in Saudi Arabia (Aljumah and Aljebreen, 2017).

Colorectal cancer control in Saudi Arabia: The way forward

More research work is highly needed to elucidate the risk factors for CRC in the Saudi population as there are very few studies carried in this field. The CRC control program should stimulate the population to adhere to a healthy life style with respect to the following:

1. Control of the body weight.
2. Quit smoking and alcohol intake.
3. Physical exercise.

4. Healthy diet.
5. Avoid stress.
6. Routine medical checkup.
7. Enrollment in CRC early detection project for the targeted groups.
8. Identification of the new cases of CRC by increasing the awareness of early detection.
9. National campaigns promoting healthy food choices, sports and fitness activities.

In conclusions, Colorectal cancer incidence in Saudi Arabia is increasing in both males and females and presents at a younger age. Research work on the identification of the risk factors to the disease must be encouraged. Moreover, further research on the threshold age for screening CRC among asymptomatic persons at average-risk in KSA is needed. Results obtained from such studies would provide evidences for the policy makers to design an evidence-based control program for CRC in KSA. There is a high need for a comprehensive CRC control program that disseminate the knowledge about the disease and stimulate the Saudi population to be enrolled in the early detection project of CRC and to adopt a healthy lifestyle in order to decrease the burden of this deadly disease. Furthermore, comprehensive longitudinal studies to identify the correlation of genetic and environmental factors with CRC incidence in KSA are needed. These studies would provide necessary data to CRC control programs in KSA aiming at disease prevention , early detection and better management options for reducing morbidity and mortality from this disease.

Author Contribution Statement

All authors participate in data collection and interpretation. NE and MMAE drafted the manuscript. All authors read and approved the final manuscript

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Not applicable.

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Competing interests
All authors declare that they have no competing interests.

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