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Distribution and Determinants of Colorectal Cancer,
Kingdom of Saudi Arabia, 2004 – 2010

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Distribution and Determinants of Colorectal Cancer, Kingdom of Saudi Arabia, 2004 – 2010

By

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Hubert Department of Global Health
2015

Abstract

Distribution and Determinants of Colorectal Cancer,
Kingdom of Saudi Arabia, 2004 – 2010
By Marei Alrouaili

Background: Colorectal cancer (CRC) is the fastest growing cause of cancer-related illnesses and deaths globally and (in particular) in the Kingdom of Saudi Arabia (KSA). The purposes of this study were to investigate trends in CRC incidence rates (IRs) from 2004 – 2010 in KSA; make recommendations for further investigation; and offer options for policy change.

Methods: We estimated the IRs and 95% confidence Intervals (CIs) of CRC in KSA from 2004 – 2010. The CRC IRs were stratified by nationality, gender, and the 13 administrative regions. IRs were estimated using the number of cases per year over the total population per 100,000 individuals.

Results: We observed a consistent increase of CRC IRs over the time period of the study. This increase of was statistically significant from 2004 (IR=4.06; 95%CI=3.79-4.32) to 2010 (IR=5.62; 95%CI=5.34-5.9), with a substantially high IR in 2009. Among Saudis, a significant increase was observed in IR from 2004 (IR=4.05; 95%CI=3.74-4.36) to 2010 (IR=6.01; 95%CI=5.66-6.36). Among non-Saudis, a similar trend was also observed in IR from 2004 (IR=3.64; 95% CI=3.17-4.12) to 2010 (IR=4.07; 95%CI=4.24-5.16). Among males, the IR increased significantly from 2004 – 2010, from 4.26 in 2004 (95%CI=3.9-4.62) to 5.68 in 2010 (95%CI=5.31-6.06). A similarly significant increase in IR was also observed among females, from 3.8 in 2004 (95%CI=3.42-4.18), to 5.55 in 2010 (95%CI=5.13-5.97). The differences in IRs by gender were not statistically significant except in the years 2005 and 2009.

Conclusion: The incidence and mortality rates can be significantly diminished through early screening and detection, healthier diet, increased amounts of physical activity, and the elimination of harmful lifestyle habits. Recommendations for further study include probing into the reasons behind the higher rates of CRC in men versus women and possibly a separate study that includes the records of patients who have been seen by private doctors. Future studies should build on the conclusions from this research in order to narrow down the individuals for whom CRC poses a higher threat and determine additional common factors between them. It is the responsibility of public health departments to ensure the health and wellbeing of the KSA residents to the best of their ability.

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ACKNOWLEDGEMENTS

First and foremost, I would like to thank my research supervisor, Dr. Scott McNabb. Without his assistance and involvement in every step of the process, this paper would never have been completed. I would also like to thank Dr. Abdullah Assiri and Dr. Haya Al-Eid very much for their support. And to the team members who stood with me at every step, Ms. Natalie Schulhofer, Mr. Suman Kundu, and Mr. Prabhjyot Saini—thank you so much.

I cannot forget my family, especially my wife, my father, and my mother, for their support and encouragement over the past 2 years. Last but not least, I would thank my best colleague, Fahad Almutairi, a close friend with whom I've spent a great deal of time studying and attending classes, someone who has been there for me when there was no one else to answer my queries.

Chapter 1

Introduction

In 2012, colorectal cancer (CRC) afflicted approximately 1.4 million people worldwide, causing nearly 693,900 deaths [1]. The highest rates of disease occur in North America and Europe and in the countries of South Korea, New Zealand, and Australia. Trends show that over the past 20 years, the incidence of CRC has decreased in these high-risk and high-income countries due to the adoption of proper and frequent screening and early detection. However, certain countries such as Spain have not followed this pattern and have seen higher rates of CRC, which could be related to high obesity rates [1]. Likewise, the rise of CRC in certain Asian countries may coincide with "Westernization" and related factors such as an unhealthy diet, obesity, and smoking [1].

CRC is a serious public health threat. According to the American Cancer Society, it is the third most commonly diagnosed cancer, as well as the third leading cause of cancer death in both men and women in the United States. In 2014 in the United States, 136,830 people were diagnosed with CRC and 50,310 people died [2]. Fortunately, screening and early detection of CRC has led to a significant reduction in mortality over the past decade. Individuals over age 50 participate less often in the CRC screenings consistent with current guidelines than younger people do [2].

CRC develops initially in the colon or rectum, organs that play an important role in the breakdown of food and its expulsion as waste. Water and various other metals are absorbed in the colon during this process, and the fecal residue remains and is expelled at a later time from the body through the anus. CRC begins as a benign enlargement or polyp on the inner lining of the colon or rectum, and with time it becomes malignant. This process can take anywhere from 10 to 20 years [2]. Because CRC has a long latency

period, screening and early detection are crucial for improving the patient's chances of survival.

At present, few reports describe the distribution and determinates of CRC in the Kingdom of Saudi Arabia (KSA), although the Saudi Cancer Registry (SCR) reported in 2005 that this type of cancer was the second most common malignancy among Saudis of all ages (10.3%) and the number one malignancy in males (11.8%) [3]. Currently, CRC is the most common cancer among men and the third most common among women in KSA [4].

These reports indicate the magnitude of CRC in KSA. Also, this information on trends indicates that CRC is on the rise among certain populations, but questions have arisen about the reasons for this and what factors are contributing to it. What factors can be analyzed and altered to reverse this trend?

The main objective of this study was to examine the incidence of CRC and its regional distribution in KSA and to propose recommendations to lower CRC incidence rates.

Many authors believe that cases of CRC in KSA will increase over the next decade because of changing dietary habits and the lack of proper screening. This is reason enough to implement a strict approach [5]. The question is, should screening start at a younger age? This question is repeatedly posed in countries witnessing similar epidemiologic results [6] [7].

Problem Statement

CRC is a significant health problem in KSA. The increase in CRC incidence rates will place a sizeable burden on the health system in KSA in the coming years. According to an analysis in the *Saudi Journal of Gastroenterology*, the number of CRC cases is expected to jump four times in the coming years. Although research on CRC in KSA

conducted from 1999 to 2003 reveals a significant increase in CRC among Saudi males (20.5%), and a small increase of 6% among Saudi females, both sexes will suffer from the impact of the problem in the coming years; the situation will progressively worsen without a more in-depth analysis of CRC causes and possible methods of prevention [5].

In addition to research on the reasons behind the different rates of CRC among males and females, work must be focused on geographical factors that contribute to this growing problem in order to create the proper methods to prevent and control it. Factors such as the environment and food trends certainly make a difference in the tendency of many diseases, and CRC is no exception. CRC seems to effect the younger generation of Saudis. For this reason, factors to take into consideration include not only gender but specific age groups as well, as "this disease is affecting the young population to a greater extent with an advanced stage presentation" [8].

The scientific literature also strongly suggests that the high incidence of CRC among Saudis may be significantly linked to dietary habits, as CRC is technically a proliferation of tumors in the colon, appendix or rectum [8].

One of the major issues related to detecting CRC in KSA in general is the fact that symptoms can be considered normal and mask the seriousness of the problem. Factors and symptoms that are common indicators of CRC tend to be within the range of normal bodily functions, such as diarrhea and constipation, and can go unchecked for long periods of time [8]. Late detection seems to be due to the similarity of the gastrointestinal symptoms and warning signs for other commonplace diseases that people may have. When severe signs (like bleeding) present themselves, it is important that the patient go and see a doctor as soon as possible and increase the chances of early detection and survival. If CRC is left unchecked, it will progress quickly to the later stages. Once CRC reaches a certain stage, it may become very difficult to treat.

Purpose of Project

The purpose of this research is to study the epidemiology of CRC in the Saudi Arabian population. Our goal is to explore reasons behind the large number of cases that are detected late and to collect more information about factors that may influence the IR and distribution of CRC cases. A number of factors could be associated with the CRC in KSA, including age, gender, regional distribution, and nationality. The aim of this study is to identify these risk factors and the role each plays individually and in combination. This study was a retrospective analysis of all CRC cases registered in the Saudi Cancer Register (SCR) between 2004 and 2010. Our intention is to analyze trends and identify patterns of CRC cases in KSA, and most importantly, to recommend interventions.

Research Questions

- Is the IR of CRC higher in certain regions?
- Is there a difference in the number and types of CRC among men and women?
- What measures are being taken to prevent and control CRC?
- What can be done to further promote early detection?

Chapter 2

Literature Review

Global Distribution of Reported Cases of CRC

The American Cancer Society (ACS) reported in 2012 that the IR of CRC has declined over the past two decades [1]. This downward trend is evident in high-income, developed countries with adequate health care, education, detection methods, and early screening resources.

However, even as the rates of CRC decline, those of all cancers continue to grow at an alarming rate all over the world. By 2030, there are expected to be 21.7 million new cancer cases and 13 million cancer deaths that are simply a result of the increase and aging of the population. However, the future burden of cancer will likely be much greater because of the changes in lifestyle that are known to increase the risk of cancer, in developing countries such as smoking, poor diet, lack of physical activity, and fewer pregnancies [1].

ACS also reported that, based on GLOBOCAN project data, factors such as the age structure of the population in developing countries, along with the deficiency and the misuse of diagnostic tests that can lead to cancer-related infections are partially responsible for geographic differences in cancer rates and survival occurrence. The risk of diagnosis becomes greater with age, and the differences in the age distribution are attributable to the fact that there are a larger number of young people in developing countries than in developed countries [1].

A report based on 2012 GLOBOCAN data asserted that over time, cancer will become a greater burden on less-developed countries; 57% of 14.1 million new cancer cases worldwide and 65% of cancer deaths worldwide will occur in these areas [9].

Cancer prevalence and outcomes differ between low- and high-income countries. Lung cancer has the poorest chance of survival in males in developed and developing countries; it has even surpassed breast cancer as the leading cause of death in women. Other types of cancer (e.g., prostate cancer in men; cervical cancer in women; liver, stomach, and colorectal cancer in both sexes) have almost doubled in developed compared with developing countries. However, the "mortality rates are only 8% to 15% higher in developed countries [9]. According to Torre (2015), these disparities can only be explained by regional variations, treatment practices, and timely detection methods [9].

Sunkara and Hebert (2015) used a regression analysis model to decode global gaps in CRC occurrence, treatment methods, screening processes, and rates of survival. They referred to this analysis as a mortality-to-incidence ratio (MIR), and it provides an overview of survival rates in relation to cancer IRs. The study used data from nine countries and health system rankings from the WHO. The MIR was the dependent and health system ranking was the independent variable. Two linear regression models were used, one including all countries and one with the “divergents” (countries with extremely high MIRs) removed [10].

It is important to note that divergents were excluded from this study to get a more coherent understanding of the problem. The results showed that a total of nine countries had MIRs that differed from the actual MIR by more than 20%. The regression model for all countries in the study represented only 24% of the total variance MIR. What do these results mean? Following removal of the divergent factors, the regression model justified 60% of the overall MIR inconsistency. This MIR is a strong indicator of the usefulness of cancer surveillance programs that can lead to more in-depth explanations of the global factors behind incidence and mortality rates [10].

Colorectal Cancer in the United States

Colorectal Cancer Facts and Figures [2] focused on the United States, one of the most economically developed countries. These statistics identify factors that must be highlighted when investigating the regional and demographic factors behind CRC in developing countries. This article related CRC diagnoses and deaths in 2014, but most importantly, it shed light on the fact that the elderly population in the United States, like many older people elsewhere, fail to undergo regular screening for CRC in compliance with recommended guidelines. In 2010, only 59% of those ≥ 50 years old underwent screening, though it is recommended for all in that age group [2].

This report points out the demographic characteristics that are significantly associated with a risk of developing CRC. In addition to age, gender is a factor, with a 30% to 40% higher incidence and death rate among males than females. The IR of CRC is higher among minority populations, but varies significantly between them. Fortunately, CRC diminished from 2008 – 2010. These declines have been attributed to increased CRC screening and earlier removal of precancerous polyps [2].

Colorectal Cancer in Saudi Arabia

The Saudi Arabia Cancer Registry (SCR) tracked the number of cancer diagnoses in KSA in 2009 and noted that these cases had increased, possibly due to population spikes as well as case management on the part of the SCR [4]. Methods such as tumor topography and morphology were used in relation to the extent of the disease in all cases at this time. The distribution was categorized by nationality (Saudi and non-Saudi), age, and sex. For all groups, cancer incidence was reported per 100,000 population. CRC was the second most common cancer among Saudis in 2009. The report found that the 1,109 cases of CRC accounted for 11.3% of all cancer cases that year. CRC ranked

first in males at a rate of 617 cases (55.6%) and third in females at rate of 492 cases (44.4%) [4].

The report also focused more on specific aspects of the reasons behind the cancer rates in KSA. It stated that “cancer rates vary greatly with age, and the crude rate is strongly influenced by the demographic structure of the population [4]. Most importantly, the report states that lack of available data and medical records related to cancer incidence could prove to be a major obstacle in conducting research, and that the production of relevant and useful reports will lead to an improvement in this situation.

This report also included statistics on incidence and reveals the alarmingly low survival rates in comparison to the number of cases. Research shows that the overall cancer IR was higher among women than men, and it was most certainly higher among Saudis (10,095 cases) than non-Saudis (2,948 cases). The five Saudi regions with the highest Age Standardized Rate (ASR), the rate that a population would have with a standard age structure, were Riyadh (120.6/100,000), the Eastern Region (110.8/100,000), Tabuk (89.9/100,000), Makkah (87.2/100,000), and Qassin (77.4/100,000) [4]. Again, among all types of cancer, CRC had the highest IR among Saudi males and females in these regions [4].

Mahmoud S Al-Ahwal [11] offered a more specific focus on the target time period of CRC in KSA. This overall survival (OS) occurrence of CRC analysis in the 1994 – 2004 period conducted by the Cancer Registry Arabia (SCR) assembles into one report data collected from all regions of KSA using the Kaplan-Meier method to determine the cumulative survival rate in terms or gender and specific time period. Once again, it was showed that the survival rate for men (41%) was much less than the survival rate for women (51%). A cox regression analysis revealed that “age and extent were significant prognostic factors of survival in patients with colon cancer; the risk was higher in patients

with distant metastasis . . . In patients with rectal cancer, the risk was lower in males, but higher in patients with unknown tumor extent" [11]. Although the five-year OS for CRC patients was 44.6% during this time period, the conclusion was drawn based on the lower than usual OS that a national screening program must be implemented.

Mosli & Al-Ahwal [3] studied the trend of CRC IRs in Jeddah, the main urban city in western KSA; its population is 3.2 million. The SCR provided retrospective analysis in 2007 of CRC diagnoses in Jeddah during the period from January 2000 to December 2006. The SCR is a population-based registry that records all cases of cancer reported by the MoH, government and private health institutions, clinics, and laboratories all over KSA that included data on age, sex, tumor pathology, tumor location and TNM stage at the time of diagnosis for all cases of CRC diagnosed during the 6-year study period [3]. Compared with CRC patients from all parts of KSA (whose mean age < 45), participants from Jeddah (with a higher mean age) had greater IRs of CRC. Men, whose mean age was 58, had a greater CRC rate than women, whose mean age was 53. Among younger patients at the national level, the CRC IRs were much lower. Another factor was studied, the location of the tumor. CRC occurred most frequently in the rectum (24%) and sigmoid colon (16%). A total of 165 (26%) patients presented with localized disease and 160 (25%) patients had distant metastasis, while the remaining patients had various degrees of regional extension or an unknown stage [3].

A study by Ahmadi, Hashemi and Mobasheri [12] compared the variations between the survival and success of individuals diagnosed with CRC on the basis of race in Iran while also adjusting for additional indicators in terms of the chance of survival. The researchers used a bivariate, multivariate analysis and Cox regression methods in this study. The study took place from 2008 – 2012 and 1127 patients from public as well as private hospitals participated [12]. A total of 61% of the study

participants were male, and there was ethnic variation among them. The ethnicities of the patients were Fars, Turciks, Kurds, Lurs, and others, in order of ratio of participation. The risk ratio among these groups varied, and other variables were included, such as tumor stage and grade, marital status, gender, education, family history of CRC, and smoking habits. The results indicated that race, ease of access to health care and, importantly, other socioeconomic factors, were reliable predictors of survival and prioritization in most cases CRC.

A study by Mansoor, Zahrani & Abdul-Aziz [13] details a histopathological profile for CRC at King Abdul Aziz Hospital in Jeddah and compares it with other studies from KSA. The study consisted of 39 patients with CRC during the time period from January 1996 to December 2000. Out of 2552 gastrointestinal endoscopic specimens collected during a 4-year period, 276 were colorectal specimens [13]. The results showed a higher frequency of cases occurring at younger ages, which can be prevented by early detection and screening.

Demographic and Risk Factors for Saudi population

The Impact of Stratifying by Family History in Colorectal Cancer Screening Programs, by Goede et al. [14] studied the cumulative number of CRC deaths compared with early detection based on the family history of the disease. Patients who had at least one relative previously diagnosed with CRC were included in the study, and they ranged in age from 50 – 74 years old. It was conjectured that nearly 11% of the population had a family history of CRC. As indicated by this study, family history is a significant risk factor of CRC and is one of the criteria that early screening should be based upon [14].

Tandon, Imam, Ismail, & Castro [15] discussed the fact that CRC had become much more manageable and that there has been a decline in mortality rates with the implementation of early screening and detection. The problem, they write, lies in

convincing the patient to take the responsibility to participate in the screening process. Lack of funds and resources are also major issues, even in developed countries. Therefore, it is necessary to identify the factors that may indicate the predisposition of certian individuals to develop CRC. Body Mass Index (BMI) is one of the critical factors. This study concludes that BMI, waist-to-hip ratio, and waist circumference have been linked to higher risk of colon polyps, which are often associated with and indicative of CRC [15].

Davis et al. [6] studied CRC patients aged 20 – 49 from 1987 – 2006 to determine tumor locations and CRC incidence for this age range. The study showed that the advanced CRC cases in the 35 to 49 year age group greatly surpassed that of the 40 to 44 year age group, but the most significant augmentation of cases was seen in the latter. CRC incidence was higher in 2006 than in 1987 across all age groups. The disease increased most significantly among those age 40 to 44, when it went from a low of 10.7 per 100,000 in 1988 to 17.9 per 100,000 in 2006 [6]. Results concluded that CRC screening should ideally begin no later than 40 years of age.

Ganapathi et al. [7] conducted a study of clinopathologic traits, OS, and disease-free survival (DFS) of 2,538 total patients under the age of 40 years and older patients in various stages of CRC over a span of 20 years. They hypothesized that the worst consequences of CRC in younger patients is associated with the advanced stage of the disease at the time of diagnosis and sub-par differentiation. Kaplan-Meier, Cox regression, and log rank models were used for the performance of the survival analysis [7]. The study concluded that the invasion of blood vessels and the high proportion of T4 rates negatively affect the survival rates in younger CRC patients.

Gaduputi et al. [16] conducted a study that identified large inconsistencies in screening modalities for Hispanic and American CRC patients based on socioeconomic

status. The patients received routine colonoscopies for CRC indications from 2003 to 2013, and patients with histories of insufficient bowel preparations were left out of the study. After being divided into three high CRC risk groups and a control group based on personal history of adenomatous polyps, family history, and general high risk based on various other factors, they received specific instructions on bowel preparation. They were rated in terms of good, fair, poor, and inadequate bowel preparation [16]. The study concluded that bowel preparations were poorer in participants with adenomatous polyps in spite of ethnicity, but it also took into account that the remaining participants produced good or fair bowel preparations due to adherence to instructions.

Amin et al. [17] investigated demographic markers of CRC in patients presenting symptoms of the disease and histopathologic features in KSA's Al Hassa region. During 2012, CRC was the first and third male most commonly occurring cancer among male and female in the KSA, and it has been steadily rising in terms of the age standardized rate (ASR). However, despite the increase in CRC rate, there are regional variations and fewer cases in the Arab world in comparison with Western countries [17]. According to the study, this gap is narrowing rapidly due to an increase in predisposing factors along with a decrease in protective mechanisms. The study concluded that the more urbanized regions of KSA produced higher CRC cases in relation to ASR due mainly to changing factors in the environment, in addition to other factors such as gender, age, and family history. The authors also concluded that despite the previously mentioned regional variation, CRC diagnosis among patients aged 40-50 was significantly greater than in Western countries.

Factors Most Important for Improved CRC Survival Rates

An study by Azam [8] enhanced and reinforced the realization that the growing number of CRC cases in younger people in KSA should have been discovered earlier.

Again, early screening and detection can help prevent these diagnoses at late stage of the disease, and certain clinical and demographic factors influence the outcomes. CRC is the third most common cancer in the world and affects young people to a greater extent with advanced stage presentation. Overall, 63% of the total cancer cases were diagnosed at stage III and stage IV, which is why public health education and screening programs for those under 40 is so important for reducing the rate of the disease [8].

Ibrahim et al. [5] looked at the CRC problem in KSA by examining lifestyle factors as well as the growth and aging of the population, specifically from 1994 to 2003. According to a 2003 report on KSA cancer incidence quoted in the study, KSA is considered a low-incidence area for CRC (ranking second after breast cancer). CRC makes up 9% of the newly diagnosed cases and is the cancer with the highest incidence among men and third highest among women [5].

The study surmised that geographical differences in CRC IR can probably be attributed to dietary changes accompanying immigration and exposure to unfamiliar environmental factors along with increased body fat and low physical activity rates. The higher IRs of CRC cases among men can probably be attributed to an increase in the number of cases among the whole population due to a more Westernized way of life. Again, these IRs can be reduced or lowered through earlier screening and detection.

CRC Prevention Strategies

It is clear that specific demographic factors such as location (region), age, gender, and nationality are the elements that come into play and make a difference in the diagnosis and mortality rates and improved chance of survival after CRC. Age and developmental stages of CRC seem to go hand in hand, so KSA must modify its CRC screening process and regulations in order to promote early detection, which will lead to higher survival rates. Factors such as age, sex, lifestyle choices, and especially family

history are useful in determining which individuals are more at risk for developing CRC. Accurate updating and transferral of patient records will show gaps and deficiencies in medical history reporting for patients seen in hospitals versus those who seen by private doctors, so all data should be included for observation in order to give a clearer picture of this issue.

Limitations to Achieving Better CRC Prevention

Based on the literature, the limitations to achieving better CRC prevention are susceptibility of certain age groups, lack of funding, predisposing genetic factors, lifestyle habits and inaccurate record keeping. Certain limitations can possibly be controlled, such as funding, healthier ways of living, and early screening/detection. However, other gaps are uncontrollable, such as genetic factors and CRC cases that are not publicly reported by private doctors at the patients' request.

Chapter 3

Manuscript

Incidence and Regional Distribution of Colorectal Cancer in Saudi Arabia, 2004 — 2010

Abstract

Objectives: Colorectal cancer (CRC) is currently the fastest growing cause of cancer-related incidences and deaths globally and particularly in the Kingdom of Saudi Arabia (KSA). The purpose of this study is to investigate the trends in CRC incidence from 2004 – 2010 among the KSA population, make recommendations for further investigation, and offer recommendation for policy changes.

Methods: We estimated the incidence rate (IR) per year and 95% confidence Interval (CI) of CRC for the KSA population from 2004 – 2010 to investigate the trend of IRs. The CRC IRs were stratified by nationality, gender, and 13 administrative regions. IRs were estimated using the number of cases per year over the total population per 100,000 individuals.

Results: We observed a consistent CRC increase of IR. The increase of IR was statistically significant from 2004 (IR=4.06; 95%CI=3.79-4.32) to 2010 (IR=5.62; 95%CI=5.34-5.9), with a substantially high IR in 2009. Among Saudis, a significant increase was observed in IR from 2004 (IR=4.05; 95%CI=3.74-4.36) to 2010 (IR=6.01; 95%CI=5.66-6.36). Among non-Saudis, a similar trend was also observed in IR from 2004 (IR=3.64; 95% CI=3.17-4.12) to 2010 (IR=4.07; 95%CI=4.24-5.16). Among males, the IR increased significantly from 2004 – 2010, from 4.26 in 2004 (95%CI=3.9-4.62) to 5.68 in 2010 (95%CI=5.31-6.06). A similarly significant increase in IR was also observed among females, from 3.8 in 2004 (95%CI=3.42-4.18), to 5.55 in 2010 (95%CI=5.13-5.97). The differences in IRs by gender were not statistically significant except in the years 2005 and 2009.

Conclusion: The CRC incidence and mortality rates can be significantly diminished through early screening and detection, healthier diet, increased amounts of physical activity, and the elimination of harmful lifestyle habits. Recommendations for further study include probing into the reasons behind the higher rates of CRC in men versus women and possibly a separate study that includes the records of patients who have been seen by private doctors. Future studies should build on the conclusions from this research in order to narrow down the individuals for whom CRC poses a higher threat and determine additional common factors between them. It is the responsibility of public health departments to ensure the health and wellbeing of the KSA residents to the best of their ability.

Introduction

In 2005, the population of the Kingdom of Saudi Arabia (KSA) was estimated at 16,945,484, composed mostly of native Saudis (62%). In that same year, the Saudi Cancer Registry (SCR) reported that colorectal cancer (CRC) was the second most common malignancy among Saudis for all ages (10.3%) and the number one malignancy in males (11.8%) [3]. At present, very few reports provide a descriptive epidemiology of CRC in KSA, which in general can indicate the magnitude of cancer care in the Kingdom [13] [5].

In 2008, some authors expect that there will be an increase CRC incidence rate (IR) in KSA during the next decade due to possible westernization of our dietary habits and lack of proper screening, which is also another reason to implement such a strict approach [5]. Whether or not we should start screening at a lower age is another question, which has been repeatedly brought up in other countries with similar epidemiological observation [6] [7].

Colorectal cancer (CRC) is a major health problem in KSA. We sought to describe the distribution of CRC in KSA. Thus, this study examined the incidence and regional distribution of CRC in KSA from 2004 – 2010.

Methods

A retrospective analysis of all cases of CRC recorded in the Saudi Cancer Registry (SCR) between 2004 and 2010 was conducted to estimate the IRs and 95% confidence Intervals (CI) of CRC in KSA from 2004 – 2010. We estimated the IRs stratified by nationality, gender, and 13 administrative regions. We excluded 98 patients for whom no region was specified. CRC IRs were estimated using the number of cases per year over the total population per 100,000 individuals. We used the Chi-square test

to determine the statistical difference between the IRs of male and female case patients, and Saudi and Non-Saudi nationals. Corresponding p-values were reported.

Two sources of population data were used. First, the data from Central Department of Statistic (CDS) were used to estimate the IR for the total population and by nationality and gender. Second data from Ministry of Health (MoH) were used to calculate the IR by administrative regions since the region level data were not accessible through the CDS database. Cases data were obtained from SCR (a population-based registry that began January 1994). The SCR database comprised all cancer cases reported to the MoH, governmental and private hospitals as well as clinics and laboratories throughout the country.

We performed Chi-square tests to investigate the relationship between tumor location and age dichotomizing it below and above 45 years of age. A p-value of less than 0.05 was considered statistical significance. Descriptive and analytic statistics were performed using Microsoft Excel 2011 (Microsoft, Seattle, WA). This analysis was determined to be IRB-exempt because it used secondary data and all data were de-identified prior to analysis. Prior to data collection, all portions of the study were reviewed by Emory‘s IRB and determined to be exempt from human subject’s review.

Results

We observed an increasing trend in the IR of CRC in KSA, by year. (Table 1). This increase was statistically significant from 2004 (IR=4.06; 95%CI=3.79-4.32) to 2010 (IR=5.62; 95%CI=5.34-5.9). The CRC IRs of Saudis was consistently higher than that of non-Saudis. (Table 2) Among Saudis, we observed a significant increase in IR from 2004 (IR=4.05; 95%CI=3.74-4.36) to 2010 (IR=6.01; 95%CI=5.66-6.36). A similar trend was observed for non-Saudis from 2004 (IR=3.64; 95%CI=3.17-4.12) to 2010 (IR=4.07;

95%CI=4.24-5.16). The difference in IRs by nationality was statistically significant for all years of the study period except 2004 and 2006.

We observed a significant increase in CRC IRs from 2004 to 2010 for both males and females. (Table 3) For males, the IR was 4.26 (95%CI=3.9-4.62) per 100,000 population in 2004 and gradually increased to 5.68 (95%CI=5.31-6.06) in 2010. A similar trend was observed for females, whose IR was 3.8 (95%CI=3.42-4.18) in 2004, increasing to 5.55 (95%CI=5.13-5.97) in 2010. The difference in IR by gender was generally not statistically significant during the study period except in the years 2005 and 2009. We observed a consistently greater CRC IR in Makkah and Riyadh regions, (Figure 1) and lower IRs in the regions of Jazan and Northern Borders. (Figure 2) Among both males and females, the proportion of cases was much higher for those > 45 years of age. (Figure 3) We also performed a Chi-square test to investigate the relationship between age groups of < and > 45 years old and tumor location, and the relationship was significant (p-value =0.02).

Discussion

We observed a steadily increasing number of CRC cases and IRs over the study period (except for 2009); a similar upward trend was observed by nationality and gender. The CRC IR among Saudis was greater than that among non-Saudis, and males had a greater IR than females. The CRC IRs in Riyadh, Makkah, and Eastern Region were greater than that of the total population, and the proportion of CRC cases was much greater in those > 45 years of age.

One reason for the higher CRC IRs among Saudis (in comparison to non-Saudis) might be underreporting. Non-Saudis often do not have proper health insurance and they may be afraid of deportation or may prefer to receive treatment in their home country. Our findings revealed that CRC IRs were much higher in men than women; this should

be a crucial aspect for future research. Higher IRs in Riyadh, Makkah and the Eastern Region might be attributed to a more Westernized way of life; this should be tested too.

The study's main limitations were due to poor record keeping and lack of access to the medical records of patients seen by private doctors. Inclusion of these individuals on future research and studies may very well provide important answers.

The results of our study strongly suggest that early detection and adherence to recommended screening methods are crucial in reducing the rates of CRC cases. Frequent screenings can lead to detection of precancerous polyps that can be safely removed before the patient develops CRC especially in men younger age. Promoting health education about the prevalence of CRC, especially in regions with greater IRs, and about the importance of early detection is essential. In addition, encouraging a healthier lifestyle and higher levels of physical activity may have a positive impact. Finally, keeping accurate records of patients, their habits, and the medical histories of their families in order to provide reliable data would allow researchers to better identify areas that could be improved in the fight against this disease.

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Table 1. Reported Cases of Colorectal Cancer and Incidence Rates, by Year, Kingdom of Saudi Arabia, 2004 – 2010

Year	#	IR°	95% CI*
2004	915	4.06	3.79 - 4.32
2005	1051	4.51	4.23 - 4.78
2006	1061	4.40	4.13 - 4.66
2007	1172	4.70	4.43 - 4.97
2008	1246	4.83	4.56 - 5.10
2009	1477	5.54	5.26 - 5.82
2010	1550	5.62	5.34 - 5.90
Total	8472		

°IR = incidence rate per 100,000 population
*CI = confidence interval

Table 2. Reported Cases of Colorectal Cancer and Incidence Rates, by Year and Nationality, Kingdom of Saudi Arabia, 2004 – 2010

Year	**Saudi**			**Non-Saudi**			**p-value**
	#	IR°	95% CI*	#	IR°	95% CI*	
2004	666	4.05	3.74 - 4.36	223	3.64	3.17 - 4.12	0.17
2005	789	4.68	4.35 - 5.01	249	3.85	3.37 - 4.32	<0.05
2006	772	4.47	4.15 - 4.79	272	3.97	3.50 - 4.44	0.09
2007	864	4.88	4.56 - 5.21	292	4.03	3.57 - 4.49	<0.05
2008	926	5.11	4.78 - 5.44	310	4.04	3.59 - 4.49	<0.05
2009	1143	6.16	5.81 - 6.52	324	3.99	3.56 - 4.43	<0.05
2010	1140	6.01	5.66 - 6.36	404	4.70	4.24 - 5.16	<0.05
Total	6,300			2,074			

°IR = incidence rate per 100,000 population
*CI = confidence interval

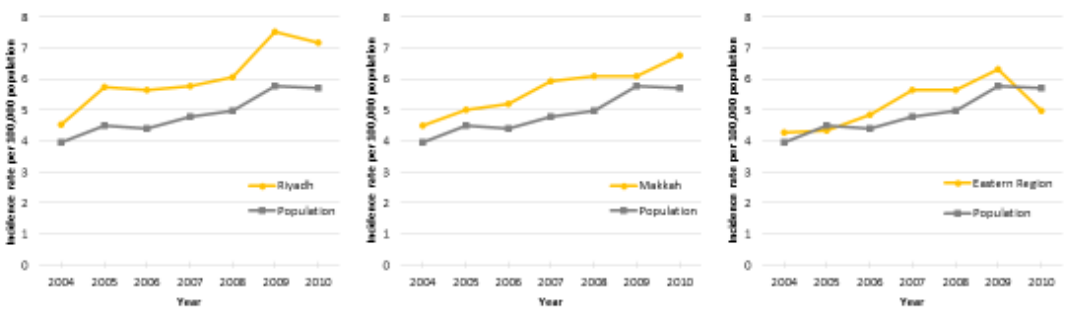
Table 3. Reported Cases of Colorectal Cancer and Incidence Rates, by Year and Gender, Kingdom of Saudi Arabia, 2004 – 2010

Year	Male			Female			p-value
	#	IR°	95% CI*	#	IR°	95% CI*	
2004	532	4.26	3.90 - 4.62	383	3.80	3.42 - 4.18	0.09
2005	629	4.85	4.47 - 5.23	422	4.07	3.68 - 4.46	<0.05
2006	592	4.40	4.05 - 4.76	469	4.39	3.99 - 4.79	0.97
2007	674	4.83	4.47 - 5.20	498	4.53	4.13 - 4.93	0.27
2008	714	4.93	4.57 - 5.30	532	4.70	4.30 - 5.10	0.40
2009	875	5.83	5.44 - 6.21	602	5.17	4.76 - 5.58	<0.05
2010	885	5.68	5.31 - 6.06	665	5.55	5.13 - 5.97	0.65
Total	4,901			3,571			

°IR = incidence rate per 100,000 population
*CI = confidence interval

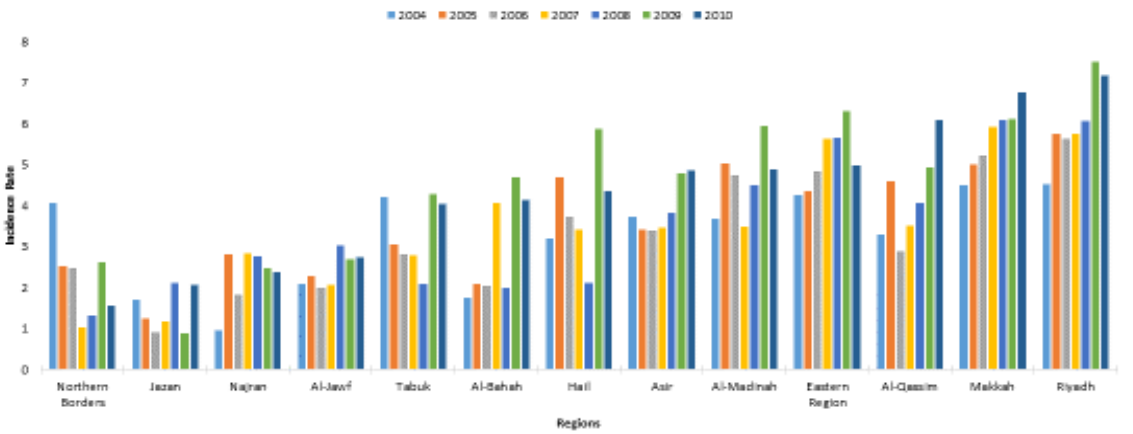
Figure 1. Incidence Rates° of Reported Cases of Colorectal Cancer, by Year and Region, Kingdom of Saudi Arabia, 2004 – 2010

(Regions with a greater incidence rates than the total population each year for at least 4 out of 6 years)



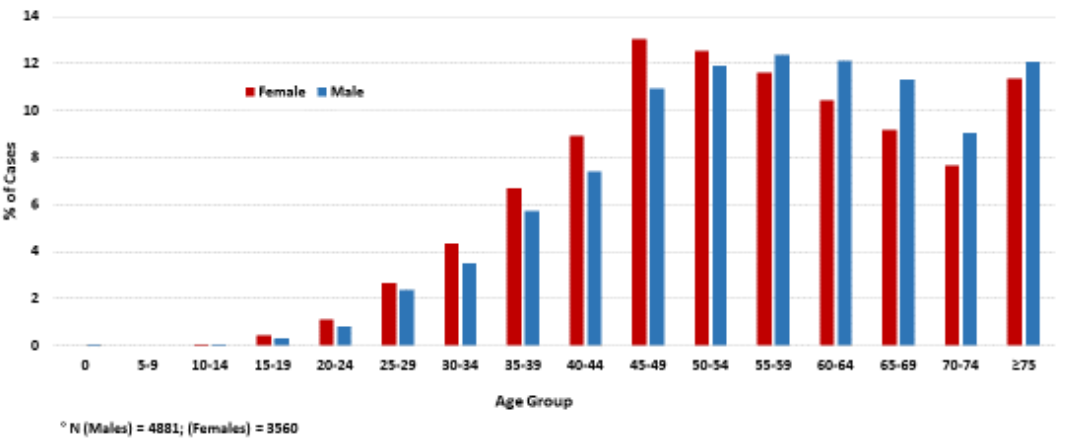
Riyadh Makkah Eastern Region

Figure 2. Reported Incidence Rates of Colorectal Cancer, by Year and Region°, Kingdom of Saudi Arabia, 2004 – 2010



° data ordered by increasing IR in 2010

Figure 3. Proportion of Reported Cases° of Colorectal Cancer, by Age and Gender, Kingdom of Saudi Arabia, 2004 – 2010



° N (Males) = 4881; (Females) = 3560

Chapter 4

Conclusion

The main purpose of this study was to analyze the CRC IRs for the period 2004 – 2010 to determine the distribution of this health outcome by nationality, gender, and region. CRC IRs increased in KSA over the study period. There were specific demographic factors such as location/region, age, nationality, and gender that seemed to impact diagnosis, mortality rates, and improved chances of CRC survival.

The scientific literature indicates that this regional variation is probably linked to dietary and environmental elements and lifestyle, which is consistent with the initial observation at the beginning of this study. A growing tendency towards a Western diet over the years could possibly be one of the reasons for the increase in CRC; although mortality rates in the West are similar to KSA because of a lack of focus on the importance of early detection and screening, CRC is actually more common in the Western world. As far as the differences in the number of CRC cases within the KSA, population spikes in more urban areas could explain the higher IR per 100,000 of the population in certain regions.

In both Saudi and non-Saudi populations, men had consistently higher IRs than women regardless of age, region, or family history. For that matter, the distribution of morphological CRC in KSA is much higher in terms of percentage in men than in women, particularly with regard to adenocarcinoma NOS. Our findings from this study provide limited evidence as to exactly why CRC rates are so much higher in men than women. Along with a higher IR, males also had lower rates of CRC survival in comparison to females. This finding deserves further research.

Measures that are currently being taken in order to gain better control of this problem include encouraging members of the younger population to participate in early

screening and possibly early detection in order to increase overall chances of survival. Unfortunately, socioeconomic status and funding are issues along with education about the importance of this type of screening. Additional measures that can and should be taken are awareness of any types of cancer in family history and accurate record keeping, dietary and lifestyle changes such as healthier food choices and increased physical activity and avoidance of harmful habits such as smoking. Other factors on which to focus further research are gender, age, region and ethnicity.

Limitations

The study's main limitations of poor record keeping and lack of access to the medical records of patients seen by private doctors. Inclusion of these individuals on future research and studies may very well provide important answers.

Recommendations

Overall, the results of our study strongly suggest that early detection and adherence to recommended screening methods are crucial in reducing the rates of CRC cases. As mentioned in the literature review, frequent screenings can lead to detection of precancerous polyps that can be safely removed before the patient develops CRC. It is important to begin screening at younger ages, especially among men, as indicated by the higher rates of CRC in the elderly population.

Based on these results, health care professionals in KSA should be focused in their efforts to promote education about the prevalence of CRC in this region and the importance of early detection. In addition, they should also encourage a healthier lifestyle and higher levels of physical activity. Most importantly, health care professionals must keep accurate records of these patients, their habits, and the medical histories of their families in order to provide reliable data allowing researchers to identify areas that could be improved in the fight against this disease.

Future studies should include the records of patients who are seen and treated by private physicians. Including these records in the current statistics may provide useful information about survival rates and may further strengthen the evidence of the benefits of regular screening and early detection. Second, future studies should investigate more deeply the reasons behind the higher IR among men overall. Is it a hormonal issue, or is it perhaps a lifestyle or dietary issue? Perhaps it is simply a genetic problem. Answers to these questions could help lower CRC IRs not only in KSA, but all over the world. Moreover, a deeper investigation into the importance of bowel preparation may be useful.

From the public health perspective, we must change or update policies in order to address the issue of CRC in KSA. It is clear that it is a major problem, and despite the public's slowly increasing awareness, measures must be taken in order to promote screening and early detection that will save lives and preserve the health of the growing population.

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Appendix

Table 1 (Appendix). Morphological Distribution of Colorectal Cancer in Saudi Arabia, 2004-2010

Morphology	Female (%)	Male (%)	Total (%)
Adenocarcinoma in tubulovillous adenoma	0.8	1.1	1.9
Adenocarcinoma in villous adenoma	0.8	1.1	1.8
Adenocarcinoma, NOS	31.6	42.6	74.2
Carcinoma, NOS	0.6	1.0	1.6
Mucinous adenocarcinoma	3.4	4.9	8.3
Mucin-producing adenocarcinoma	0.8	1.4	2.2
Papillary adenocarcinoma, NOS	0.2	0.4	0.6
Signet ring cell carcinoma	0.9	1.5	2.5
All Others	3.1	3.9	7.0
Grand Total	**42.2**	**57.8**	**100.0**