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Original Article

Colorectal carcinoma in Western Libya: a Retrospective Study on Libyan Patients treated at Subrata National Cancer Institute (SNCI) in 2024

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Abstract

Background: Cancer is an important health concern in Libya, especially in the setting of an aging population and limited healthcare facilities. Colorectal cancer (CRC) is one of them. The prevalence of CRC in the world has demonstrated a notable upward trend in recent years, ranking as the second most common cancer among men and the third among women. This research aims to study CRC in the western region of Libya in terms of some non-modifiable risk factors such as age, gender, regional distribution, and genetic predisposition**. Method and Methods:** A retrospective descriptive study was conducted involving 202 individuals diagnosed with colorectal cancer at the Subrata National Cancer Institute (SNCI) in 2024, aiming to represent colorectal cancer among Libyan patients. **Results:** Overall, cancer was more prevalent among males than females; it affected 113 (55.9%) males and 89 (44.1%) females. 149 (73.8%) of all recorded cases were found in coastal areas, the area documented the highest percentage of all cases found in the western region of Libya. About 43.1% of patients were >60 years old, followed by 33.7% within the age group of 51-60 years old. In this study, patients presented with anemia, with mean hemoglobin levels appearing lower in females compared to males. 24.2% of patients have a positive family history of CRC, and only 5.4% have a positive family history of colorectal polyps.. **Conclusion:** The current Libyan CRC cohort shows that the average age at diagnosis was more than 60 years, with a male gender predominance. All patients presented with low hemoglobin levels. CRC occurred more frequently in coastal areas than in mountainous areas in Libya's western region.

Keywords: Colorectal cancer, age, sex, family history of CRC, family history colorectal polyps, regional di

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INTRODUCTION:

Worldwide, colorectal cancer (CRC) ranks as the third most frequently diagnosed cancer and stands as the second highest cause of cancer-related deaths, with more than 1.9 million new cases and 0.9 million deaths in 2020. [1-3] There are significant geographic differences in the incidence and mortality rates of colorectal cancer among various countries around the world according to GLOBOCAN data in 2020. [4] Many studies indicates that the most substantial increases in colorectal cancer (CRC) incidence and mortality are observed in countries with medium to high Human Development Index (HDI) scores. This trend is frequently associated with the societal adoption of lifestyle patterns characteristic of 'Western' cultures. [5] These disparities in CRC may reflect variations in exposure to its associated risk factors, encompassing lifestyle and environmental determinants. The primary preventive measures for CRC, involves identifying and addressing modifiable risk factors, especially lifestyle-related elements (e.g., alcohol consumption, smoking, obesity, unhealthy dietary patterns), as well as enhancing protective factors (e.g., physical activity, specific pharmacological interventions such as aspirin, and adoption of a healthy diet [6, 7]. Age represents a primary non-modifiable risk factor for colorectal cancer (CRC) incidence. Individuals exceeding 50 years of age exhibit a markedly heightened risk, comprising upwards of 90% of all CRC diagnoses. Globally, males demonstrate a higher burden of colorectal cancer (CRC), with an Age-Standardized Rate (ASR) of 23.4 per 100,000, in contrast to 16.2 per 100,000 in females, yielding a male-to-female incidence ratio of 1.4. Notably, the sex differential in CRC incidence, as reflected by this ratio, is greater within high-income settings (1.4) than in low-income settings (1.2) [8, 9].

North Africa presents the highest regional age-standardized incidence rates (ASIR) for colorectal cancer (CRC) within Africa. The ASIR was estimated at 8.2–8.66 per 100,000 population in 2022, nearly double the continental mean. In this region, CRC incidence has demonstrated a steady increase over the past decades, likely driven by increasing urbanization, adverse lifestyle modifications (including obesity, smoking, and sedentary behavior), and improvements in diagnostic infrastructure and detection [10,11].

Despite limited age-stratified data, reports indicate a significant early-onset colorectal cancer (EOCRC) burden in North Africa, paralleling global trends.

For example, Algeria exhibits rapidly rising CRC incidence with increasing diagnoses among younger cohorts, likely reflecting evolving risk factor profiles. [12] Consistent with global epidemiology, most CRC diagnoses occur in individuals≥ 50 years. Tunisian ASIR significantly increased from 6.4/100,000 (1994) to 12.4/100,000 (2009). [13] In Libya the mean age of CRC diagnosis is approximately 58.7 years. with males diagnosed slightly younger (57.3y) than females (60.1y). Libyan CRC incidence and ASR shows an upward trend; for example, Southern Libya cases increased (2016-2018) becoming the second malignancy post-breast cancer. Libya ranks high in North Africa with ASRs (as of 2012 data) around 17.5/100k (males) and 17.2/100k (females) with Higher urban incidence that suggests lifestyle and diagnostic access factors [14-16].

The predominant hereditary colorectal cancer (CRC) syndromes include familial adenomatous polyposis (FAP), stemming from germline mutations in the APC gene, [17, 18]. And Lynch syndrome, which is associated with germline mutations in DNA mismatch repair (MMR) genes [19, 20].

Although individuals harboring these germline mutations face a substantially increased risk of CRC, such inherited predispositions collectively account for approximately 5% of all CRC incidences [19, 21]. Notably, a higher proportion (16%) of inherited syndromes has been reported in early-onset CRC (EOCRC) cases. Recent genome-wide association studies (GWAS) have identified novel genetic variants associated with CRC risk, thereby highlighting the imperative for further investigation to elucidate their clinical implications. [22, 23].

These findings suggest that future resequencing efforts may facilitate the identification of rarer, low-frequency variants [22]. The increased risk of colorectal cancer (CRC) among first-degree relatives (FDRs) of patients, with relative risks (RRs) between 2 and 4, is a well-documented finding across numerous studies employing varied methodologies and diverse populations [17,19]. As such, a family history of CRC, [17,19, 24, 25]. Or adenomatous colonic polyps in FDRs constitute an important risk factor, integral to the identification of high-risk cohorts for targeted interventions outlined in CRC prevention guidelines and control strategies [26, 27]. Significant advances in understanding CRC etiology and chemotherapeutic treatment have not always resulted in corresponding improvements in patient survival outcomes. The

efficacy of surgical intervention in CRC is highly reliant on the tumor's stage and innate biological characteristics. Indeed, early-stage CRC can frequently be definitively controlled and cured with surgical excision as a monotherapy [28]. Metastasis significantly worsens the patient's prognosis, with a 5-year survival rate of less than 5%. For the majority of patients, chemotherapy can enhance survival and is the predominant modality of treatment in these individuals [29].

Overall, the incidence of colorectal cancer in Middle Eastern countries is lower than that in Western ones [30]. due to a number of challenges. For Libya, Relatively there is a little data available about CRC. In a local study conducted in Benghazi, Elzouki et al. 2005 discovered no significant differences between gender, location, or type of CRC. The majority of CRC patients in Benghazi were diagnosed at a late stage, with either locally progressed or metastatic illness [31].

A unique research opportunity is presented to Libyan patients at the Subrata National Cancer Institute, the second largest tumor treatment center in Libya, in the western region, which many cancer patients are diagnosed and treated. The aim of this study is to find data on colon cancer, including its relationship with age, sex, hemoglobin level and, as well as to know if there is a relationship between the family history of cancer, genetic factors, and the occurrence of tumors.

MATERIALS AND METHODS:

This study's methodology is based on a cohort of 202 confirmed colorectal cancer cases, which were carefully selected according to specific inclusion criteria to ensure data accuracy and reliability, following ethical approval from the hospital authority. Data from this sample, comprising individuals from various age groups and genders, were classified into key variables including age groups, gender distribution, hemoglobin levels, and family history of either colorectal cancer (CRC) or colorectal polyps. To assess these variables, specific statistical methods were employed: independent two-sample t-tests were used to compare continuous variables, such as hemoglobin levels across gender groups, while Chi-Square tests were conducted to evaluate associations between categorical variables. A significance level of $p < 0.05$ was applied to determine the statistical relevance of all observed relationships. Collectively, these analyses aim to provide a deeper understanding of the factors contributing to colorectal cancer, thereby supporting the development of more precise prevention strategies and diagnostic approaches.

RESULT:

This study examined a cohort of 202 colorectal cancer cases, revealing several key characteristics. The data indicates a higher prevalence of colorectal cancer among males **(55.9%)** compared to females **(44.1%)** within this cohort, a finding that aligns with some existing literature suggesting a potential gender disparity in colorectal cancer incidence. Both sexes presented with low hemoglobin level (anemia). In female patients, the mean hemoglobin levels appeared lower compared to male patients, a finding that aligns with many preexisting researches.

A substantial proportion of the cohort **(24.2%)** reported a positive family history of colorectal cancer, highlighting the potential role of genetic predisposition in the development of the disease. In contrast, a family history of polyps was relatively uncommon in this cohort, with only **(5.4%)** reporting a positive history. This may suggest that while a family history of colorectal cancer is a notable risk factor, a family history of polyps alone may not be as strongly associated with colorectal cancer development in this particular sample, though patient recall bias and incomplete family history information may influence these findings.

The age distribution data reveals that colorectal cancer is predominantly diagnosed in older age groups within this cohort. The majority of cases were observed in individuals over 50 years of age, with the **>60** age group representing the largest proportion **(43.1%).** This is consistent with the established understanding that age is a significant risk factor for colorectal cancer.

Data analysis:

Figure 1 presents the gender prevalence among the 202 CRC cases examined in this study. The results indicate that CRC was more prevalent among males (55.9%) than females (44.1%) within this specific cohort. This observation warrants further investigation to explore potential gender-related risk factors or biological mechanisms that might contribute to this difference in prevalence.

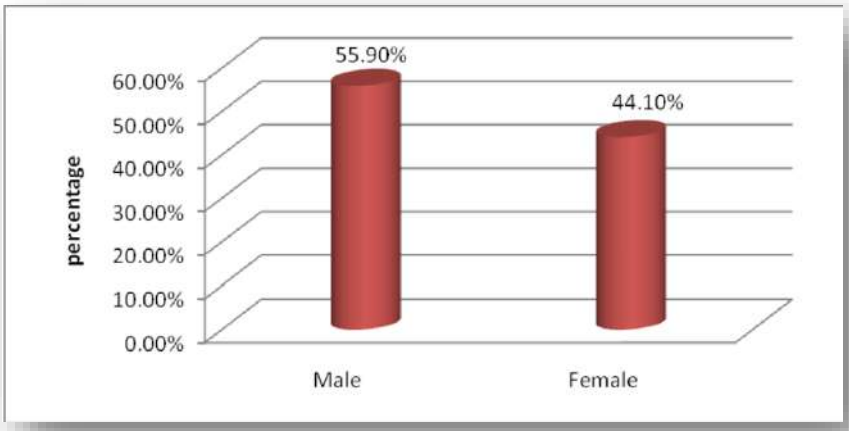

Figure 1: Gender-Specific Prevalence of CRC within the Study Cohort

Figure 2 presents the age distribution within the study sample of CRC cases. The most frequent age group was > 60 years, accounting for 43.1% of the cases (87 individuals). The 51-60 age group represented 33.7% of the cases (68 individuals), followed by the 41-50 age group at 14.4% (29 individuals). The smallest proportion of cases was observed in individuals ≤ 40 years, representing 8.9% of the sample (18 individuals). This distribution suggests that, within this cohort, the disease is more frequently diagnosed in older age groups.

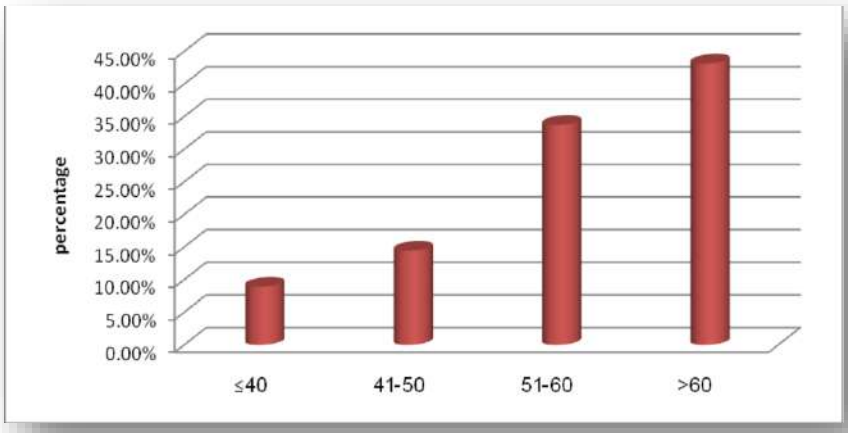

Figure 2: Age Distribution among CRC Cases

Figure 3 presents the mean hemoglobin (Hb) levels along with the standard deviation for male and female patients diagnosed with colorectal cancer. An independent two-sample t-test was conducted to determine if there is a statistically significant difference between the two groups.

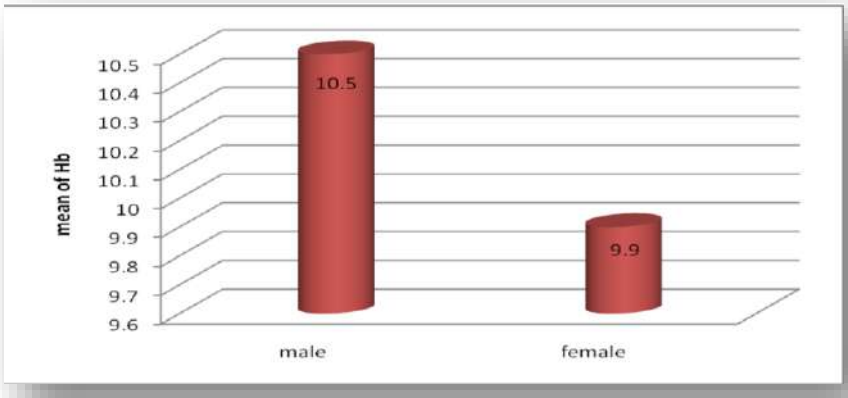

Figure 3: Hemoglobin levels by gender, CRC cases

Figure 4 show that the CRC patient in this cohort presented with mean Hb level of (10.5 ± 1.7 for male and 9.9 ± 1.5 for female), whereas the main first complaint of most colorectal cancer patients is symptoms and signs of anemia, indicating that most cases are diagnosed in advanced stages of the disease. The mean hemoglobin levels appear lower in females compared to males. However, the p-value (0.361) from the independent t-test suggests that this difference is not statistically significant at the conventional threshold ($p > 0.05$).

Figure 4 , examines the percentage of patients with a family history of CRC (positive or negative) within the study cohort. Overall, 24.2% (49 cases) reported a positive family history, while 75.8% (153 cases) reported no family history of the disease.

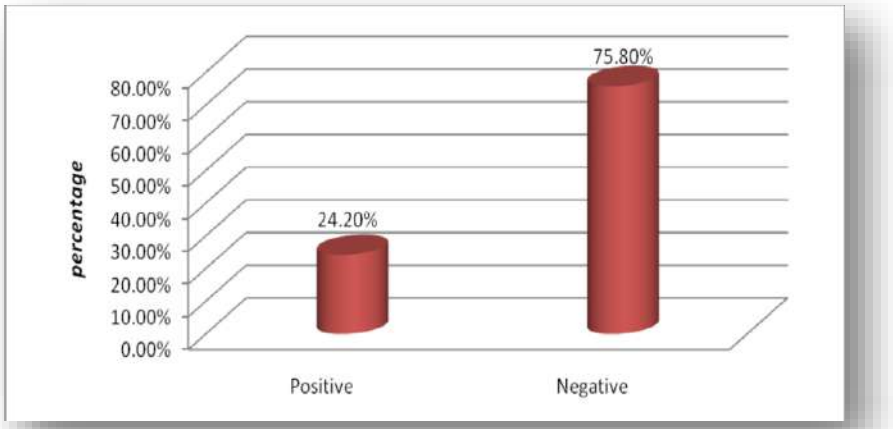

Figure 4: Percentage of family history in CRC cases

Figure 5 presents the percentage of patients with family history of colorectal polyps among the CRC cases in this study. A small percentage, 5.4% (11 cases), reported a positive family history of polyps, while the vast majority, 94.6% (191 cases), reported a negative family history. Further analysis is needed to determine if this low prevalence of reported family history of colorectal polyps has any association with other clinical or demographic factors in this cohort.

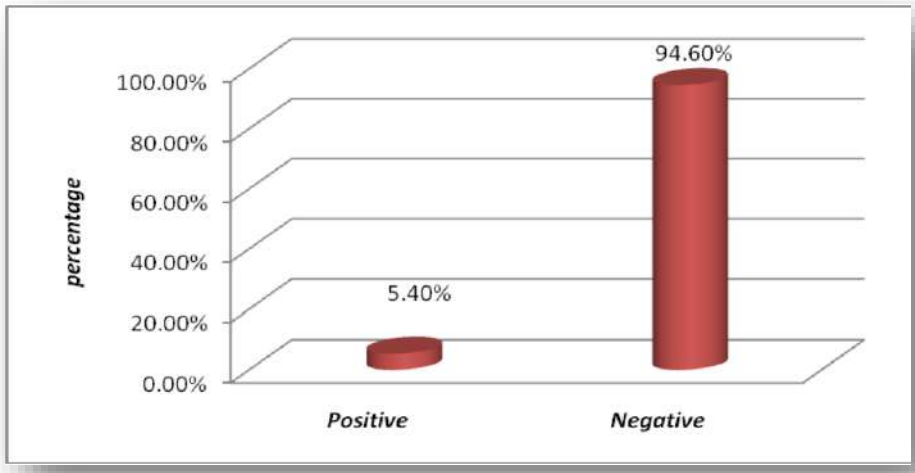

Figure 5: Distribution of colorectal cancer cases by family history of polyps

Figure 6 shows a dominance of coastal areas: with 149 cases (approximately 73.8%**),** the coastal areas exhibit a notably higher incidence of colon cancer compared to the mountain areas, lower incidence in

mountain areas the mountain areas accounted for only 53 cases (about 26.2%**).**

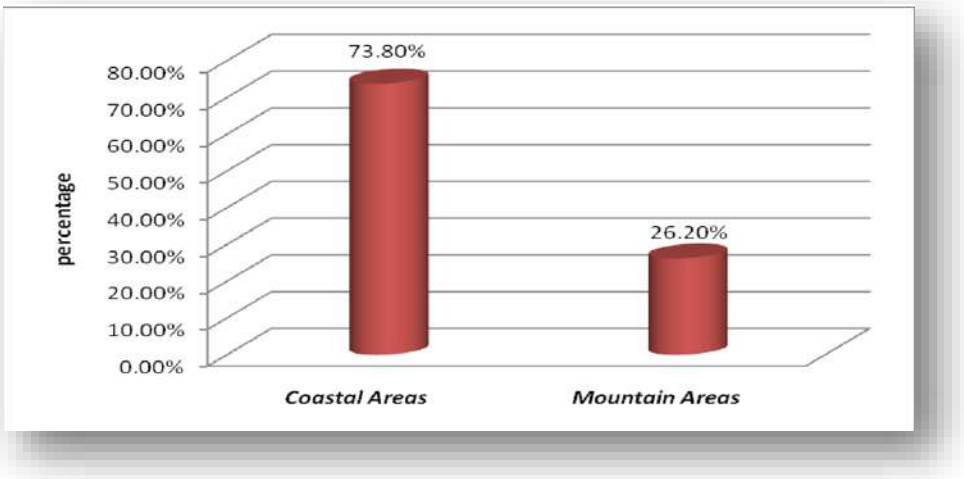

Figure 6: Regional distribution of CRC

In summary, this study provides valuable insights into the characteristics of colorectal cancer cases within this specific context. The findings highlight the importance of considering gender, family history of colorectal cancer, and age as potential factors influencing the development of the disease.

DISCUSSION:

CRC is a set of heterogeneous diseases with variable genetic and biological mechanisms indicating various tumor characteristics and outcomes. [32] This type of carcinoma affects both sexes, but males are affected more in contrast to females. [33] A higher incidence of CRC is observed in developed countries relative to developing nations, demonstrating significant geographical disparities. The highest rates are reported in Europe, Australia, and the United States, contrasting with the lowest rates in Africa and South-Central Asia [34, 35]. The present cohort performed a detailed retrospective analysis of 202 patients with CRC diagnosed and treated at the National Cancer Institute, Subrata, Libya. The sociodemographic and biological variables including (age, sex, address and blood hemoglobin level), as well as family history of CRC and family history of colorectal polyps were analyzed. Age is a significant determinant in the etiology of colorectal cancer (CRC). Previous research consistently demonstrates a marked increase in CRC incidence among individuals aged 50 years and older [36, 37]. Consistent with this finding, our analysis showed that the most age category impacted by CRC was 51-60 years (33.7%). Our result is in an agreement whit those reported in Libya and others developing countries ,and are much higher than in western countries [38-42] .Also, Many Western researchers found that more than 80% of CRC cases afflict adults over the age of 50, which matches our findings [36].

Our analysis shows a significant sex difference between male and female patients, namely, (55.9%) men and (44.1%) women, which is in agreement with GLOBOCAN 2018 data that states that men are more likely to develop colorectal cancer than women. [43] Many previous studies stated that male sex can increase the chance of developing colorectal cancer due to various biological and lifestyle reasons [44, 45]. Males tend to drink more alcohol and smoke more cigarettes [46-48]. And they are more likely to store fat in their abdomen, which raises their chances of developing colorectal cancer when compared to females. [49] Additionally, many earlier research efforts have indicated that testosterone could encourage the development of colorectal tumors [50, 51] . On the other hand, it has been noted that estrogen might help protect against the occurrence of colorectal cancer, which could explain why women tend to have lower rates of this disease [52]. Many previous studies showed that CRC is affected by both genetic and environmental factors, whereas hereditary CRCs constitute around 5% of all CRC cases. Familial adenomatous polyposis and lynch syndrome are

hereditary syndromes have a significantly elevated risk of CRC [53-55]. While the incidence of CRC in the general population is around 6%, people with a positive family history are at a much higher risk. Individuals with a family history of CRC are 2 to 4 times more likely to develop CRC than those without a family history. This elevated risk is due to the inheritance of defective genes passed down from one generation to the next, highlighting the role of genetics in cancer development [56, 57]. Previous researches revealed that the risk of developing CRC is roughly 1.8-1.9 times higher in patients with a positive family history in a first-degree relative, highlighting the necessity for better diagnostic approaches for these patients. [58-60] In our study, of 202 of CRC patients a 49 individuals (24.2%) have a positive family history of CRC, and 11 individuals (5.4%) have a positive family history of colorectal polyposis: these results are in agreement with the above mentioned information. Since subjects with a positive family history of cancer are considered high-risk for developing CRC, early detection and medical attention are critical to improving prognosis. Guidelines propose expanded screening interventions for these people to ensure timely detection and treatment [61]. The incidence and mortality of colorectal cancer (CRC) vary greatly by country throughout the world. [62] With the highest incidence rates in Australia and New Zealand, Europe, and the USA, and the lowest rates in Africa and South-Central Asia, the regional incidence of colorectal cancer ranges by more than ten times [63]. This regional disparities appear to be caused by food and environmental exposure variances as well as a genetic predisposition[64, 65]. In general, Middle Eastern nations have a lower incidence of colorectal cancer than Western nations [66].

This study revealed that 149 (73.8%) of patients registered at SNCI were from coastal areas of western Libya, and 53 (26.2%) were from mountain areas. The variation in food types and exposure to environmental pollution may explain these differences in regional distribution among the western Libyan population. This disparity necessitates further research to pinpoint the specific pollutants that could be contributing to the higher rates of colorectal cancer (CRC) in certain areas compared to others, particularly in regions close to sources of petroleum emissions, which are prevalent in the Zawia city due to its oil refinery. CRC in Libya , was found to be the leading malignancy in males and the second most prevalent among females [67]. Genetic predisposition, the increasing Westernization of eating habits in Libya, physical inactivity, and the lack of screening programs may be significant predisposing factors. However, the exact causes of this unusually high occurrence remain unclear.

CONCLUSION:

CRC is a disease that presents with nonspecific symptoms. This study could serve as a roadmap to increase awareness of the need for early screening for CRC and the necessity of promoting healthier lifestyle choices as a means of primary prevention. A national program for the prevention of CRC should be developed to address this issue, taking into account the necessary measures to overcome the various challenges such programs may face in developing countries like Libya. It is suggested to adopt a comprehensive screening program for those most at risk of developing this tumor, those living in areas with high environmental pollution, and those who are individuals from families with a history of polyps or CRC. This approach mirrors advanced communities where screening has proven effective in the early diagnosis of the disease and in modifying the years of disease progression. It is proposed to integrate the national prevention program for colon and rectal cancer at the primary care level, specifically through primary healthcare centers spread throughout the country.

REFERENCES:

1- Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. Transl Oncol. 2021 Jul;14(10):101174. doi:10.1016/j.tranon.2021.101174. PMID: 34243011; PMCID: PMC8273208.

2- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021

May;71(3):209-249. doi:10.3322/caac.21660. PMID: 33538338.
3- Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, Bray F. Cancer statistics for the year 2020: An overview. Int J Cancer. 2021 Apr 5. doi: 10.1002/ijc.33588. Epub ahead of print. PMID: 33818764.
4- Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, Vignat J, Ferlay J, Murphy N, Bray F. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. Gut. 2023 Feb;72(2):338-344. doi: 10.1136/gutjnl-2022-327736. Epub 2022 Sep 8. PMID: 36604116.
5- Sung H, Siegel RL, Rosenberg PS, Jemal A. Emerging cancer trends among young adults in the USA: analysis of a population-based cancer registry. Lancet Public Health. 2019 Mar;4(3):e137-e147. doi: 10.1016/S2468-2667(18)30267-6. Epub 2019 Feb 4. PMID: 30733056.
6- Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. CA Cancer J Clin. 2023 May-Jun;73(3):233-254. doi: 10.3322/caac.21772. Epub 2023 Mar 1. PMID: 36856579.
7- Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2020. CA Cancer J Clin. 2020 May;70(3):145-164. doi: 10.3322/caac.21601. Epub 2020 Mar 5. PMID: 32133645.
8- Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019 Oct 19;394(10207):1467-1480. doi: 10.1016/S0140-6736(19)32319-0. PMID: 31631858.
9- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
10- Virginie MLIL, Zhao Q, Liu L. African colorectal cancer burden in 2022 and projections to 2050. Ecancermedicalscience. 2024 Sep 26;18:1780. doi: 10.3332/ecancer.2024.1780. PMID: 39430071; PMCID: PMC11489094.
11- Arhin N, Ssentongo P, Taylor M, Olecki EJ, Pameijer C, Shen C, Oh J, Eng C. Age-standardised incidence rate and epidemiology of colorectal cancer in Africa: a systematic review and meta-analysis. BMJ Open. 2022 Jan 17;12(1):e052376. doi: 10.1136/bmjopen-2021-052376. PMID: 35039287; PMCID: PMC8765019.
12- Herrag SEE, Moulessehoul S, Mehadji DE, Yekrou D, Khaled MB. Epidemiological insights into colorectal cancer in northwestern Algeria. Ecancermedicalscience. 2024 Mar 21;18:1684. doi: 10.3332/ecancer.2024.1684. PMID: 38566765; PMCID: PMC10984843.
13- Khiari H, Ben Ayoub HW, Ben Khadhra H, Hsairi M. Colorectal Cancer Incidence Trend and Projections in Tunisia (1994 - 2024). Asian Pac J Cancer Prev. 2017 Oct 26;18(10):2733-2739. doi: 10.22034/APJCP.2017.18.10.2733. PMID: 29072401; PMCID: PMC5747397.
14- Abuderman A, Alhadi A, Alhadi M, et al. Cancer incidence in eastern Libya: First results from Benghazi Medical Center. Pan Afr Med J. 2014 May 28;18:234.
15- Bodalal Z, Azzuz R, Bendardaf R. Cancers in Eastern Libya: first results from Benghazi Medical Center. World J Gastroenterol. 2014 May 28;20(20):6293-301. doi: 10.3748/wjg.v20.i20.6293. PMID: 24876750; PMCID: PMC4033467.
16- Gusbi E, Eltaib FI, Abrahem AF, Benbubaker WM, Alhudiri IM, Al-dabea SA, et al. Cancer incidence in southern Libya: updated report from 2016 to 2018. Libyan J Med Sci. 2021;5(1):11-16. doi:10.4103/LJMS.LJMS_74_20.
17- La Vecchia S, Sebastián C. Metabolic pathways regulating colorectal cancer initiation and progression. Semin Cell Dev Biol. 2020 Feb;98:63-70. doi: 10.1016/j.semcdb.2019.05.018. Epub 2019 May 28. PMID: 31129171.
18- Jasperson KW, Tuohy TM, Neklason DW, Burt RW. Hereditary and familial colon cancer. Gastroenterology. 2010 Jun;138(6):2044-58. doi: 10.1053/j.gastro.2010.01.054. PMID: 20420945; PMCID: PMC3057468.

19- Valle L, de Voer RM, Goldberg Y, Sjursen W, Försti A, Ruiz-Ponte C, Caldés T, Garré P, Olsen MF, Nordling M, Castellvi-Bel S, Hemminki K. Update on genetic predisposition to colorectal cancer and polyposis. Mol Aspects Med. 2019 Oct;69:10-26. doi: 10.1016/j.mam.2019.03.001. Epub 2019 Mar 18. PMID: 30862463.
20- Parry S, Win AK, Parry B, Macrae FA, Gurrin LC, Church JM, Baron JA, Giles GG, Leggett BA, Winship I, Lipton L, Young GP, Young JP, Lodge CJ, Southey MC, Newcomb PA, Le Marchand L, Haile RW, Lindor NM, Gallinger S, Hopper JL, Jenkins MA. Metachronous colorectal cancer risk for mismatch repair gene mutation carriers: the advantage of more extensive colon surgery. Gut. 2011 Jul;60(7):950-7. doi: 10.1136/gut.2010.228056. Epub 2010 Dec 30. PMID: 21193451; PMCID: PMC3848416.
21- Yurgelun MB, Kulke MH, Fuchs CS, Allen BA, Uno H, Hornick JL, Ukaegbu CI, Brais LK, McNamara PG, Mayer RJ, Schrag D, Meyerhardt JA, Ng K, Kidd J, Singh N, Hartman AR, Wenstrup RJ, Syngal S. Cancer Susceptibility Gene Mutations in Individuals With Colorectal Cancer. J Clin Oncol. 2017 Apr 1;35(10):1086-1095. doi: 10.1200/JCO.2016.71.0012. Epub 2017 Jan 30. PMID: 28135145; PMCID: PMC5455355.
22- Montazeri Z, Li X, Nyiraneza C, Ma X, Timofeeva M, Svinti V, Meng X, He Y, Bo Y, Morgan S, Castellví-Bel S, Ruiz-Ponte C, Fernández-Rozadilla C, Carracedo Á, Castells A, Bishop T, Buchanan D, Jenkins MA, Keku TO, Lindblom A, van Duijnhoven FJB, Wu A, Farrington SM, Dunlop MG, Campbell H, Theodoratou E, Zheng W, Little J. Systematic meta-analyses, field synopsis and global assessment of the evidence of genetic association studies in colorectal cancer. Gut. 2020 Aug;69(8):1460-1471. doi: 10.1136/gutjnl-2019-319313. Epub 2019 Dec 9. PMID: 31818908; PMCID: PMC7398467.
23- Zhang B, Jia WH, Matsuda K, Kweon SS, Matsuo K, Xiang YB, Shin A, Jee SH, Kim DH, Cai Q, Long J, Shi J, Wen W, Yang G, Zhang Y, Li C, Li B, Guo Y, Ren Z, Ji BT, Pan ZZ, Takahashi A, Shin MH, Matsuda F, Gao YT, Oh JH, Kim S, Ahn YO; Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO); Chan AT, Chang-Claude J, Slattery ML; Colorectal Transdisciplinary (CORECT) Study; Gruber SB, Schumacher FR, Stenzel SL; Colon Cancer Family Registry (CCFR); Casey G, Kim HR, Jeong JY, Park JW, Li HL, Hosono S, Cho SH, Kubo M, Shu XO, Zeng YX, Zheng W. Large-scale genetic study in East Asians identifies six new loci associated with colorectal cancer risk. Nat Genet. 2014 Jun;46(6):533-42. doi: 10.1038/ng.2985. Epub 2014 May 18. PMID: 24836286; PMCID: PMC4068797.
24- Taylor DP, Burt RW, Williams MS, Haug PJ, Cannon-Albright LA. Population-based family history-specific risks for colorectal cancer: a constellation approach. Gastroenterology. 2010 Mar;138(3):877-85. doi: 10.1053/j.gastro.2009.11.044. Epub 2009 Dec 21. PMID: 19932107; PMCID: PMC2831153.
25- Taylor DP, Stoddard GJ, Burt RW, Williams MS, Mitchell JA, Haug PJ, Cannon-Albright LA. How well does family history predict who will get colorectal cancer? Implications for cancer screening and counseling. Genet Med. 2011 May;13(5):385-91. doi: 10.1097/GIM.0b013e3182064384. PMID: 21270638.
26- Imperiale TF, Ransohoff DF. Risk for colorectal cancer in persons with a family history of adenomatous polyps: a systematic review. Ann Intern Med. 2012 May 15;156(10):703-9. doi: 10.7326/0003-4819-156-10-201205150-00006. PMID: 22586009.
27- Song M, Emilsson L, Roelstraete B, Ludvigsson JF. Risk of colorectal cancer in first degree relatives of patients with colorectal polyps: nationwide case-control study in Sweden. BMJ. 2021 May 4;373:n877. doi: 10.1136/bmj.n877. PMID: 33947661; PMCID: PMC8083372.
28- Walker J, Quirke P. Biology and genetics of colorectal cancer. Eur J Cancer. 2001 Oct;37 Suppl 7:S163-72. doi: 10.1016/s0959-8049(01)80018-6. PMID: 11887987.
29- Christopoulou A. Chemotherapy in metastatic colorectal cancer. Tech Coloproctol. 2004 Nov;8 Suppl 1:s43-6.

doi: 10.1007/s10151-004-0108-7. PMID: 15655639.
30- Salim EI, Moore MA, Al-Lawati JA, Al-Sayyad J, Bazawir A, Bener A, Corbex M, El-Saghir N, Habib OS, Maziak W, Mokhtar HC, Seif-Eldrin IA, Sobue T. Cancer epidemiology and control in the arab world - past, present and future. Asian Pac J Cancer Prev. 2009 Jan-Mar;10(1):3-16. PMID: 19469617.
31- Elzouki AN, Alkhomsi S. Pattern of gastrointestinal tract cancer in the Eastern part of Libya. Garyounis Med J. 2005;22:27-31
32- Schneider NI, Langner C. Prognostic stratification of colorectal cancer patients: current perspectives. Cancer Manag Res. 2014 Jul 2;6:291-300. doi: 10.2147/CMAR.S38827. PMID: 25061338; PMCID: PMC4085313.
33- Pirzada MT, Ahmed MJ, Muzzafar A, Nasir IUI, Shah MF, Khattak S, Syed AA. Rectal Carcinoma: Demographics and Clinicopathological Features from Pakistani Population Perspective. Cureus. 2017 Jun 20;9(6):e1375. doi: 10.7759/cureus.1375. PMID: 28744422; PMCID: PMC5519317.
34- Merika E, Saif MW, Katz A, Syrigos K, Morse M. Review. Colon cancer vaccines: an update. In Vivo. 2010 Sep-Oct;24(5):607-28. Erratum in: In Vivo. 2010 Nov-Dec;24(6):905. Syrigos, C [corrected to Syrigos, K]. PMID: 20952724.
35- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010 Dec 15;127(12):2893-917. doi: 10.1002/ijc.25516. PMID: 21351269.
36- Mitry E, Benhamiche AM, Jouve JL, Clinard F, Finn-Faivre C, Faivre J. Colorectal adenocarcinoma in patients under 45 years of age: comparison with older patients in a well-defined French population. Dis Colon Rectum. 2001 Mar;44(3):380-7. doi: 10.1007/BF02234737. PMID: 11289284.
37- Isbister WH. Malignant neoplasia of the colon, rectum and anus at the King Faisal Specialist Hospital and Research Centre. Ann Saudi Med. 1992 Sep;12(5):429-33. doi: 10.5144/0256-4947.1992.429. PMID: 17587016.
38- Elamyal R, Kamoka H, Hashmi H. Clinico-demographic profile of colorectal cancer patients in National Cancer Institute of Sabratha–Libya. J Med Sci Clin Res. 2017;5:31123-6.
39- Zhang C, Yin S, Tan Y, Huang J, Wang P, Hou W, Zhang Z, Xu H. Patient Selection for Adjuvant Chemotherapy in High-Risk Stage II Colon Cancer: A Systematic Review and Meta-Analysis. Am J Clin Oncol. 2020 Apr;43(4):279-287. doi: 10.1097/COC.0000000000000663. PMID: 31934881.
40- Brierley JD, Gospodarowicz MK, Wittekind C, editors. TNM classification of malignant tumours. 8th ed. Oxford: John Wiley & Sons; 2017.
41- Bakeer A, Zubia N, Belhaj E. A clinical and demographic profile of colorectal cancer: one year experience of National Cancer Institute, Misrata, Libya. Libyan Int J Oncol. 2022;1(2):59-63.
42- Gado A, Ebeid B, Abdelmohsen A, Axon A. Colorectal cancer in Egypt is commoner in young people: Is this cause for alarm? Alexandria J Med. 2014;50(3):197-201.
43- Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nat Rev Gastroenterol Hepatol. 2019 Dec;16(12):713-732. doi: 10.1038/s41575-019-0189-8. Epub 2019 Aug 27. PMID: 31455888.
44- Edgren G, Liang L, Adami HO, Chang ET. Enigmatic sex disparities in cancer incidence. Eur J Epidemiol. 2012 Mar;27(3):187-96. doi: 10.1007/s10654-011-9647-5. Epub 2012 Jan 3. PMID: 22212865.
45- Cook MB, McGlynn KA, Devesa SS, Freedman ND, Anderson WF. Sex disparities in cancer mortality and survival. Cancer Epidemiol Biomarkers Prev. 2011 Aug;20(8):1629-37. doi: 10.1158/1055-9965.EPI-11-0246. Epub 2011 Jul 12. PMID: 21750167; PMCID: PMC3153584.
46- Jin EH, Han K, Shin CM, Lee DH, Kang SJ, Lim JH, Choi YJ. Sex and Tumor-Site Differences in the Association of Alcohol Intake With the Risk of Early-Onset Colorectal Cancer. J Clin Oncol. 2023 Aug 1;41(22):3816-3825. doi: 10.1200/JCO.22.01895. Epub 2023 Jun 14. PMID: 37315287; PMCID: PMC10419447.

47- Lee S, Woo H, Lee J, Oh JH, Kim J, Shin A. Cigarette smoking, alcohol consumption, and risk of colorectal cancer in South Korea: A case-control study. Alcohol. 2019 May;76:15-21. doi: 10.1016/j.alcohol.2018.06.004. Epub 2018 Jun 26. PMID: 30529018.
48- Kim I, Lee HH, Ko YJ, Chang HE, Cheung DY, Lee BI, Cho YS, Kim JI, Choi MG. Factors associated with the risk of colorectal neoplasia in young adults under age 40. Korean J Intern Med. 2022 Sep;37(5):969-978. doi: 10.3904/kjim.2021.506. Epub 2022 Jul 25. PMID: 35872626; PMCID: PMC9449198.
49- Ortega LS, Bradbury KE, Cross AJ, Morris JS, Gunter MJ, Murphy N. A Prospective Investigation of Body Size, Body Fat Composition and Colorectal Cancer Risk in the UK Biobank. Sci Rep. 2017 Dec 19;7(1):17807. doi: 10.1038/s41598-017-17997-5. PMID: 29259258; PMCID: PMC5736687.
50- Rodríguez-Santiago Y, Terrazas-Valdés LI, Nava-Castro KE, Del Río-Araiza VH, Garay-Canales CA, Morales-Montor J. Sexual dimorphism of colorectal cancer in humans and colorectal tumors in a murine model. Front Oncol. 2024 Aug 6;14:1398175. doi: 10.3389/fonc.2024.1398175. PMID: 39165688; PMCID: PMC11333323.
51- Song CH, Kim N, Nam RH, Choi SI, Yu JE, Nho H, Shin E, Lee HN, Surh YJ. Testosterone strongly enhances azoxymethane/dextran sulfate sodium-induced colorectal cancer development in C57BL/6 mice. Am J Cancer Res. 2021 Jun 15;11(6):3145-3162. PMID: 34249451; PMCID: PMC8263677.
52- Leiszter K, Galamb O, Kalmár A, Zsigrai S, Valcz G, Szigeti KA, Barták BK, Nagy ZB, Dank M, Liposits Z, Igaz P, Tulassay Z, Molnár B. Az ösztrogének lehetséges szerepe a vastagbéldaganatok kialakulásában [Potential role of estrogens in colorectal tumour development]. Orv Hetil. 2020 Apr;161(14):532-543. Hungarian. doi: 10.1556/650.2020.31674. PMID: 32223415.
53- Bhattacharya P, Leslie SW, McHugh TW. Lynch Syndrome (Hereditary Nonpolyposis Colorectal Cancer). 2024 Jun 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 28613748.
54- Menon G, Kasi A. Familial Adenomatous Polyposis. 2024 May 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30855821.
55- Mesher D, Dove-Edwin I, Sasieni P, Vasen H, Bernstein I, Royer-Pokora B, Holinski-Feder E, Lalloo F, Evans DG, Forsberg A, Lindblom A, Thomas H. A pooled analysis of the outcome of prospective colonoscopic surveillance for familial colorectal cancer. Int J Cancer. 2014 Feb 15;134(4):939-47. doi: 10.1002/ijc.28397. Epub 2013 Aug 29. PMID: 23901040.
56- Armelao F, de Pretis G. Familial colorectal cancer: a review. World J Gastroenterol. 2014 Jul 28;20(28):9292-8. doi: 10.3748/wjg.v20.i28.9292. PMID: 25071323; PMCID: PMC4110560.
57- Smith RA, von Eschenbach AC, Wender R, Levin B, Byers T, Rothenberger D, Brooks D, Creasman W, Cohen C, Runowicz C, Saslow D, Cokkinides V, Eyre H; ACS Prostate Cancer Advisory Committee, ACS Colorectal Cancer Advisory Committee, ACS Endometrial Cancer Advisory Committee. American Cancer Society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers. Also: update 2001--testing for early lung cancer detection. CA Cancer J Clin. 2001 Jan-Feb;51(1):38-75; quiz 77-80. doi: 10.3322/canjclin.51.1.38. Erratum in: CA Cancer J Clin 2001 May-Jun;51(3):150. PMID: 11577479.
58- Jung YS, Song H, Tran MTX, Park B, Moon CM. Association between A Family History of Colorectal Cancer and the Risk of Colorectal Cancer: A Nationwide Population-Based Study. J Pers Med. 2022 Sep 23;12(10):1566. doi: 10.3390/jpm12101566. PMID: 36294706; PMCID: PMC9605451.
59- Keivanlou MH, Amini-Salehi E, Joukar F, Letafatkar N, Habibi A, Norouzi N, Vakilpour A, Aleali MS, Rafat Z, Ashoobi MT, Mansour-Ghanaei F, Hassanipour S. Family history of cancer as a potential risk factor for colorectal cancer in EMRO countries: a systematic review and meta-analysis. Sci Rep. 2023 Oct 14;13(1):17457. doi: 10.1038/s41598-023-

44487-8. PMID: 37838786; PMCID: PMC10576738.
60- Wong MC, Chan CH, Lin J, Huang JL, Huang J, Fang Y, et al. Lower relative contribution of positive family history to colorectal cancer risk with increasing age: a systematic review and meta-analysis of 9.28 million individuals. Am J Gastroenterol. 2018;113(12):1819-27.10.1038/s41395-018-0271-0.
61- Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. 2021 Mar 1;116(3):458-479. doi: 10.14309/ajg.0000000000001122. PMID: 33657038.
62- Douaiher J, Ravipati A, Grams B, Chowdhury S, Alatise O, Are C. Colorectal cancer-global burden, trends, and geographical variations. J Surg Oncol. 2017 Apr;115(5):619-630. doi: 10.1002/jso.24578. Epub 2017 Feb 13. PMID: 28194798.
63- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
64- Dong W, Kim U, Rose J, Hoehn RS, Kucmanic M, Eom K, Li S, Berger NA, Koroukian SM. Geographic Variation and Risk Factor Association of Early Versus Late Onset Colorectal Cancer. Cancers (Basel). 2023 Feb 4;15(4):1006. doi: 10.3390/cancers15041006. PMID: 36831350; PMCID: PMC9954005.
65- Akimoto N, Ugai T, Zhong R, Hamada T, Fujiyoshi K, Giannakis M, Wu K, Cao Y, Ng K, Ogino S. Rising incidence of early-onset colorectal cancer - a call to action. Nat Rev Clin Oncol. 2021 Apr;18(4):230-243. doi: 10.1038/s41571-020-00445-1. Epub 2020 Nov 20. PMID: 33219329; PMCID: PMC7994182.
66- Salim EI, Moore MA, Al-Lawati JA, Al-Sayyad J, Bazawir A, Bener A, Corbex M, El-Saghir N, Habib OS, Maziak W, Mokhtar HC, Seif-Eldrin IA, Sobue T. Cancer epidemiology and control in the arab world - past, present and future. Asian Pac J Cancer Prev. 2009 Jan-Mar;10(1):3-16. PMID: 19469617.
67- Bodalal Z, Azzuz R, Bendardaf R. Cancers in Eastern Libya: first results from Benghazi Medical Center. World J Gastroenterol. 2014 May 28;20(20):6293-301. doi: 10.3748/wjg.v20.i20.6293. PMID: 24876750; PMCID: PMC4033467.