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# The relationships between Risk Factors and the changes of Histopathological of Tissue Colon Cancer in Iraq Patients

**Review Article**
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**Abstract:** The transformation of an ordinary cell into a cancerous one could be a dynamic process which often involves the approval of oncogenes as well as deactivation of tumor suppressor properties (alterations). Most changes are emptied by cellular genome dauntlessness and repair components. In any case, many genetic changes give cells an advancement advantage and unused capacities, driving to their neoplastic alter. As other cancers, like melanoma, sarcoma, and lymphoma, could affect the colon, colon cancer, also known as colon carcinoma, affects the epithelium of colon. The uncontrolled proliferation regarding colorectal epithelial cells might be a hallmark of colorectal cancer (CRC). The multistep carcinogenesis hypothesis states that pigment cells go through a sequence of atomic alterations before they become totally dangerous cells. The inactivation related to the Adenomatous polyposis coli (APC) signaling pathway is the most frequent hereditary cause of activation. The pathology of damage includes oncogene changes, tumor suppressor qualities, and probably many signaling pathways, which put cancers at risk of metastasis. In advanced nations, CRC has a high disease-specific mortality rate and impacts over a million individuals annually. Worldwide, CRC ranks 3rd in terms of the incidence in both women and men. Africa and Central and South Asia have experienced the biggest drops in CRC, whereas New Zealand, Australia, North America, and Europe have experienced highest change rates.

**Keywords**: colon cancer, Histopathological, and Risk factors

**1-Histological Structure of Colon:**

The colon comprises of a few layers that frame both as solid tube. Layers of colorectal included from inward (lumen) to external[1]

1- Mucosa layer (inward layer) comprises of straightforward columnar epithelial cells with challis cells, lamina propria, and solid mucosa.

2- Submucosa could be a layer of loose connective tissue.

3- Muscularis externa may be a layer of muscle tissue

4- The serosa layer is (external layer). Basic columnar enterocytes (epithelial lamina) have long microvilli line the surface of the mucosa, which is enclosed in a layer of bodily fluid to encourage the development of defecation[2]. Mucosa is made up of enteroendocrine cells as well as different Lieberkühnrich sepulchers with cups instead of villi. The connective tissue layer, referred to as the lamina propriae mucosae is packed with plasma cells, macrophages, and other resistant cells, while submucosa is composed of lymph hubs, blood vessels, and particularly, fat tissue. The solid layer incorporates an exceptionally particular inward circular muscle framework, though as it were the Taeniae coli basically has an external longitudinal muscle framework [3].

**2-Functions of the Colon.**

The essential work of the colon is to store defecation for a restricted period of time and to encourage its development. Roughly 1 liter of water is ingested by the colon each day in arrange to thicken the stools. In expansion, it is able to retain sodium, potassium, and chloride whereas releasing potassium into the lumen itself. It performs certain imperative capacities counting the breakdown of inedible nourishment

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substances such as cellulose, the generation of vitamin K, the incitement of intestinal peristalsis and the fortification of the safe framework by MALT[4].

**3- Histopathology of Colon Cancer:**

Several histological types of CRC are listed in the World Health Organization's (WHO) categorization system, including shaft cell, mucinous, seal ring cell, medullary adenosquamous, and undifferentiated [5].

**a-Adenocarcinoma:**

Adenocarcinomas that arise from epithelial cells regarding the colorectal mucosa account for no less than 90% of cases of CRC 5. The basis for histological tumor review is glandular development, which is a characteristic of routine adenocarcinoma. No less than 95% of the tumor in a well-separated adenocarcinoma is shaped by the organs. Decently separated adenocarcinoma appears 50-95% organ arrangement. Ineffectively separated adenocarcinoma is for the most part strong with < 50% organ arrangement[6]

**b-Mucinous Adenocarcinoma:**

More than half of tumor mass in this rare kind of CRC is made up of extracellular mucin 5 (Hamilton et al., 2010). Tumors having a significant amount of mucinous, either as mucinous separation or mucinous highlights. Mucinous adenocarcinoma usually presents as a large glandular mass with extracellular mucin pools. Patients with Lynch disease or hereditary non-polyposis colorectal cancer (HNPC) may develop multiple mucinous adenocarcinomas[7].

**c- Seal Ring Cell Adenocarcinoma:**

Seal ring cell adenocarcinoma, which accounts for less than 1% of all CRCs, is rare in the colorectum in contrast to stomach cancer. Seal ring cell carcinoma is comparable to mucinous carcinoma in that it is defined by presence of more than half tumour cells which exhibit seal ring cell highlights, which are distinguished by prominent intracytoplasmic mucin vacuole which pushes core to the edge [8].

**d-Medullary Carcinoma:**

Medullary carcinoma is highly rare, accounting for just 5-8 incidences out of each 10000 cases of CRC that have been studied 9. Epithelioid cell sheets with large vesicular cores, abundant cytoplasm, and discernible nucleoli are the hallmarks of the tumor. It is characterized by a pushing boundary on resection examples and is associated with lymphocytes that have been verified to invade tumors.

**4-Clinical Highlights and Conclusion of CRC**

There could be a wide extent of side effects that patients may portray, however, guided addressing and fitting examination can regularly lead to a brief list of differential analyses [10]. The side effects of CRC are not intrinsically one of a kind. Patients may display with mysterious or symptomatic iron deficiency, shinning ruddy blood per rectum, stomach torment, an alter in bowel propensities, anorexia, weight misfortune, sickness, spewing, or weakness. Taken in segregation, most of these signs and side effects are not one or the other touchy nor particular and may be shown similarly in kind and threatening infections[11].

**Investigations**

Colonoscopy is the examination of choice. Be that as it may, progressively CT colonography is utilized within the examination of modified bowel propensity. It has comparable symptomatic precision to colonoscopy, in spite of the fact that clearly needs the advantage of empowering symptomatic biopsy or catching of adenomas[11]. Double-contrast barium bowel purge is utilized when colonoscopy is contra-shown. It appears a cancer of the colon as a steady unpredictable filling imperfection. Winding CT is especially valuable in elderly patients when differentiate douches or colonoscopies are not symptomatic or are contraindicated. With the appearance of innovation in this field, there has been the presentation of virtual colonoscopy, which is viable in picking up polyps down to a measure of 6mm

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**5-Epidemiology:**

CRC is a potentially fatal disease that is quite common. In the US, an estimated 132700 new cases get examined each year, 93.090 of which are colon cancer and the remaining portion are rectal cancers 12. As reported by ICR in 2010, CRC is sixth among the top ten most prevalent cancers among Iraqi patients. A study on gastrointestinal cancer in Iraqi patients revealed that there were 973 cases overall, with 973 of those being female. Despite being the second most common cancer after breast cancer in several of the wealthier Arab countries, rectal and colon cancer rates are very low. Yemen has a rather high rate of early-onset cancers (19.3%); the majority of cases have been in patients under 40 years old 15. The most frequently impacted site in Qatar is the sliding and sigmoid colon 16. CRC is not unusual among Egyptian patients who have colonoscopy procedures. Patients under 40 years old have somewhat higher rates of CRC compared to those reported in the West 17. Palestine has a high proportion of mucinous and badly differentiated people.

**6. Colorectal cancer risk factors**

Numerous established factors are known to either lower or raise colon cancer risk. A few of such variables can be changed, others cannot. A. Family history and heredity. A higher survival percentage for families affected by CRC may be attributable to early detection and greater awareness [18].

a- Hereditary non-polyposis colorectal cancer (HNCC):

A well-defined hereditary condition that produces colon cancer affects approximately 5% of persons with the disease 19. The most prevalent of such is Lynch syndrome, which has the highest risk of CRC and is referred to as HNCC (e.g., gastric, endometrial, and ovarian). [20].

**b. Familial adenomatous polyposis (FAP):**

The most prevalent predisposing genetic syndrome is familial adenomatous polyposis, which is typified by development of hundreds to thousands of the colorectal polyps in afflicted people 21. By the age of (40) [22], the lifetime risk of CRC approaches 100% if no intervention is taken. Lynch syndrome affects roughly 1 in 35 people with colon cancer [23].

**1 - Personal medical history:**

Rectal or colon cancer is more common in individuals who have had colon cancer. A higher risk is linked to a younger age at diagnosis [24]. The main tumor's anatomical location affects the risk's size as well [25].

**2- Adenomatous polyps:**

Colon cancer risk is increased by a history of adenomatous polyps. This was particularly true in the case when there have been multiple polyps or when polyps were large. It appears that having an adenoma in the family raises the risk, even though further study is required in this area [27].

**B- Chronic inflammatory disease:**

A person's chance of developing colon cancer rises with severity and length of their chronic inflammatory bowel disease (IBD), a condition where the colon becomes inflamed over an extended time period[28]. Ulcerative colitis and Crohn's disease are the 2 most prevalent IBD types. Within 30 years, colon cancer is predicted to strike 18% of ulcerative colitis patients [29].

**C- Diabetes**

Numerous studies have demonstrated that patients who have diabetes are more likely to acquire colon cancer[30]. While a sedentary lifestyle and obesity are prevalent risk factors for both adult-onset (type 2) diabetes and colon cancer, this connection persists in the case when BMI, physical activity, and waist circumference are considered [31]. According to certain research, the relation could be stronger in men compare to it in women[32].

**Risk factors for D behavior**

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**1 - Physical inactivity**

Physical exercise can be defined as one of the behavioral factors that has been linked to colon cancer risk the most frequently. The most physically active persons have 25% lower colon cancer risk when compared to the least active people, according to a recent analysis of scientific literature [33]. Conversely, people with less active colon cancer are more likely to pass away from the disease compared to those with more active colon cancer [34].

**2. Overweight and obesity**

Being overweight or obesity is associated with an increased colon cancer risk in both women and men, with stronger correlations more frequently seen in males compared to in women [36]. CRC risk is increased by being overweight or obese, regardless of physical activity. In both women and men, abdominal obesity (as determined by the size of the waist) seems to be a more significant risk factor compared to general obesity[37]. Between 1997 and 2012, the percentage of adult US citizens who were obese rose from 19% to 29% [37]

**3. Diet**

Lifestyle and diet have a significant impact on colon cancer incidence, as evidenced by geographic variations in the disease's incidence and temporal variations in risk in immigrant groups. The risk of rectal and colon cancers is increased by high diet of processed and/or red meat. Although the exact causes of this correlation are unknown, high-temperature cooking of red meat releases substances known as carcinogens. Nitrite additions and/or long-term use for food preservation [38].

**4. Smoking**:

The International Agency for Research on Cancer stated in a November 2009 report that there is enough data to draw the conclusion that smoking is a cause of colon cancer 39. Compared to colon cancer and several molecular subgroups of both rectal and colon cancer, the connection seems to be higher in rectal cancer 40. Due to the very long period of latency —at least 3 to 4 decades—between colon cancer diagnosis and tobacco smoking, it is believed that early research missed this association.

**5. Alcohol**

Alcohol use, both heavy and moderate, was linked to colon cancer. Throughout their lifetime, persons who consume two to four alcoholic drinks on average have 23% increased risk of colon cancer compared to the ones who consume fewer than 1 drink daily [41].

**6. Medicines:**

The incidence of colon cancer is significantly decreased by long-term, regular usage of aspirin and other NSAIDs 42. Research suggests that postmenopausal hormone users had a decreased colon cancer risk when compared to nonusers.

**4. Competition:**

When put to comparison with white patients of the two sexes, African Americans have highest CRC rates with regard to both incidence [43] and total mortality [44]. The latest study's authors postulated that etiological variables like smoking or diabetes could be responsible for such variations.

**6. Age:**

Colon cancer could strike anyone at any age, but as people age, their risk grows dramatically. Patients over 50 receive a diagnosis in almost 90% of colorectal cases [45].

**7. Radiation**

The dangers of depleted uranium (DU) in the body are its chemical toxicity and radioactivity. DU mainly emits alpha radiation, although beta and gamma radiation are also emitted by uranium decay products[46]. Inside the body, alpha radiation can disrupt cellular processes and damage DNA, which can increase the risk of various cancers. In the years after the 1991 Gulf War, Iraqi doctors reported an increase in cancer [47]Radiation is a stronger source of cancer when combined with other carcinogens such

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as radon exposure and smoking. Radiation can cause cancer in most parts of the body, in all animals, and at all ages. Prenatal radiation has a tenfold effect[48].

**7. Phase**

- Stage 0: the tumor is limited to the mucous membrane; cancer in situ
-1. stage: the tumor penetrates the mucosa
Stage T2: The tumor invades the outer mucosa

**8. Stage of Colorectal Cancer:**

The cancer cells' grade reveals how abnormal or normal they are. Differentiation is the process by which a normal cell becomes specialized for its function and location in the body as it matures and grows. The American Joint Commission on Cancer[49].recommends the following guidelines for grading tumors to grades 0-3 when anaplasia increases as follows:

1 - Grade 1 (low grade) - Because cancer cells are highly differentiated, they resemble normal cells in appearance.

2 - Grade 2 (moderate) - Due to their mild differentiation, cancer cells have a more atypical appearance.

3 - Grade 3 (high grade) - Because cancer cells are not well differentiated, they have an unusual appearance.

**2-Molecular Events in Relation to Colon Carcinogenesis**

There is most likely a far greater somatic mutations' spectrum which contribute to CRC pathogenesis. Two findings suggest that genes may play a role in the likelihood of acquiring CRC: there are two types of families affected by CRC: (1) those having a family history of the disease; and (2) the ones where multiple family members have been diagnosed with inherent CRC [50].

Adenomas apparently grow faster to become carcinomas in MSI tumors rather than in stable microsatellite tumors. MSI tumors display marked histological changes, such as increased secretion of mucin, which indicate that the histological characteristics of the tumors are attributable to at least some molecular occurrences [51]. There are many steps involved in the build-up of mutations in anti-oncogenes and oncogenes that lead to the development of colorectal cancer.

**p53 Mutations and Human Cancer:**

Missense, allelic losses, and frameshifi mutations are examples of p53 genetic changes found in human tumors. While nonsense mutations often cause a shortened protein product for disrupting other tumor suppressor genes, the majority of p53 mutations involve substitution alterations which prevent the protein from binding to DNA or activating gene [52]. The most common genetic changes in human tumors, which include CRC, are mutations in TP53 gene. No less than half of all human cancers, including CRC [53], have p53 mutations. It was proposed that the higher frequency of TP53 mutations in tumors situated in distal colon as opposed to proximal colon is due to variations in aetiology of CRC [54]. It has been noted that mutations that convert purines to pyrimidines, as opposed to those that transition purines to pyrimidines, are more common in distal colon tumours. As previously mentioned, mutations in colorectal adenomas are rather uncommon (16% in adenomas vs. 40–50% in CRC); these changes in the gene indicate a late event in the evolution of adenocarcinomas [55].

**References:**

**1 -** Gartner, L. P. and Hiatt, J. L. (2012). Color atlas and text of histology. Lippincott Williams and Wilkins.

2-Mescher, A. L. 2010. Junqueira's basic histology: text & atlas. McGraw- Hill Medical New York.

ISSN NO: 2770-2936
Date of Publication:11-12-2023

**3-** Welsch, U. (2006). Sobotta Lehrbuch Histologie mit StudentConsult-Zugang: Zytologie, Histologie, Mikroskopische Anatomie. Student Consult. Elsevier, Urban and FischerVerlag.

4-Schünke, M., Schulte, E. and Schumacher, U. (2009). Prometheus–LernAtlas der Anatomie: Innere Organe. Illustrationen von M. Voll und K. Wesker, Stuttgart: Thieme.

5-Hamilton S.R., Bosman F.T., Carmeiro F., Hruban R.H. and Boffetta P. (2010). Carcinoma of the colon and rectum in: WHO classification of tumors of the digestive system. Thesis MD, eds. Lyon: IARC press. 134-46.

6-Compton, C. C., Fielding, L. P., Burgart, L. J., Conley, B., Cooper, H. S., Hamilton, S. R., Hammond, M. E. H., Henson, D. E., Hutter, R. V. and Nagle, R. B. (2000). Prognostic factors in colorectal cancer. Arch Pathol Lab Med 124(7): 979-994.

7-Leopoldo, S., Lorena, B., Cinzia, A., Luciana, B. A., Renato, C., Antonio, M., Carlo, S., Cristina, P., Stefano, C. and Maurizio, T. (2008). Two subtypes of mucinous adenocarcinoma of the colorectum: clinicopathological and genetic features. Annals of surgical oncology 15(5): 1429-1439.

8-Chen, J.-S., Hsieh, P.-S., Chiang, J.-M., Yeh, C.-Y., Tsai, W.-S., Tang, R., Changchien, C.-R. and Wu, R.-C. (2010). Clinical outcome of signet ring cell carcinoma and mucinous adenocarcinoma of the colon. Chang Gung Med J 33(1): 51-57

9-Thirunavukarasu, P., Sathaiah, M., Singla, S., Sukumar, S., Karunamurthy, A., Pragatheeshwar, K. D., Lee, K. K., Zeh, H., Kane, K. M. and Bartlett, D. L. (2010). Medullary carcinoma of the large intestine: a population based analysis. International journal of oncology 37(4): 901-907.

10- Bailey, H. R. (2013). Colorectal surgery. http://www.clinicalkey.com/dura/browse/bookChapter/3-s2.0-C20090420579

11-Rowan,W. and Parks. (2012). principals and practice of surgery 6th ed., Elsevier Ltd

12-Siegel, R. L., Miller, K. D. & Jemal, A. (2015). Cancer statistics, 2015. CA: a cancer journal for clinicians 65(1): 5-29

13- Iraqi cancer registry, (2010). Republic of Iraq, Ministry of Health cancer board.

14-Mohandas, K. (2011). Colorectal cancer in India: controversies, enigmas and primary prevention. Indian Journal of Gastroenterology 30(1): 3-6.

ISSN NO: 2770-2936
Date of Publication:11-12-2023

15-Basaleem, H. O. and Al-Sakkaf, K. A. (2004). Colorectal cancer among Yemeni patients. Characteristics and trends. Saudi medical journal 25(8): 1002-1005

16-Rasul, K. I., Awidi, A. S., Mubarak, A. A. and Al-Homsi, U. M. (2001). Study of colorectal cancer in Qatar. Saudi medical journal 22(8): 705-707.

17-Gado, A., Ebeid, B., Abdelmohsen, A. and Axon, A. (2014). Colorectal cancer in Egypt is commoner in young people: Is this cause for alarm? Alexandria Journal of Medicine 50(3): 197-201.

18-Morris, E., Penegar, S., Whitehouse, L., Quirke, P., Finan, P., Bishop, D., Wilkinson, J. and Houlston, R. (2013). A retrospective observational study of the relationship between family history and survival from colorectal cancer. British journal of cancer 108(7): 1502-1507.

19-Lynch, H. T. and de la Chapelle, A. (2003). Hereditary colorectal cancer. N Engl J Med 348(10): 919-932.

20-Win, A. K., Lindor, N. M., Young, J. P., Macrae, F. A., Young, G. P., Williamson, E., Parry, S., Goldblatt, J., Lipton, L. and Winship, I. (2012). Risks of primary extracolonic cancers following colorectal cancer in lynch syndrome. Journal of the National Cancer Institute: p351.

21-Jasperson, K. W., Tuohy, T. M., Neklason, D. W. and Burt, R. W. (2010). Hereditary and familial colon cancer. Gastroenterology 138(6): 2044-2058.

22-Galiatsatos, P. and Foulkes, W. D. (2006). Familial adenomatous polyposis. The American journal of gastroenterology 101(2): 385-398.

23-Hampel, H., Frankel, W. L., Martin, E., Arnold, M., Khanduja, K., Kuebler, P., Clendenning, M., Sotamaa, K., Prior, T. and Westman, J. A. (2008). Feasibility of screening for Lynch syndrome among

24-Mysliwiec P.A., Cronin K.A. and Schatzkin A. (2006). Chapter 5: New Malignancies Following Cancer of the Colon, Rectum, and Anus. New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000. Bethesda, MD: National Cancer Institute.

25-Phipps, A. I., Chan, A. T. and Ogino, S. (2013). Anatomic subsite of primary colorectal cancer and subsequent risk and distribution of second cancers. Cancer 119(17): 3140-3147.

26-Schatzkin, A., Freedman, L. S., Dawsey, S. M. and Lanza, E. (1994). Interpreting precursor studies: what polyp trials tell us about large-bowel cancer. Journal of the National Cancer Institute 86(14): 1053-1057.

27-Imperiale, T. F. and Ransohoff, D. F. (2012). Risk for colorectal cancer in persons with a family history of adenomatous polyps: a systematic review. Annals of internal medicine 156(10): 703-709.

28-Bernstein, C. N., Blanchard, J. F., Kliewer, E. and Wajda, A. (2001). Cancer risk in patients with inflammatory bowel disease. Cancer 91(4): 854-862.

ISSN NO: 2770-2936
Date of Publication:11-12-2023

29-Eaden, J., Abrams, K. and Mayberry, J. (2001). The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48(4): 526-535.

30-Campbell, P. T., Deka, A., Jacobs, E. J., Newton, C. C., Hildebrand, J. S., McCullough, M. L., Limburg, P. J. and Gapstur, S. M. (2010). Prospective study reveals associations between colorectal cancer and type 2 diabetes mellitus or insulin use in men. Gastroenterology 139(4): 1138-1146.

31-Larsson, S. C., Giovannucci, E. and Wolk, A. (2005). Diabetes and colorectal cancer incidence in the cohort of Swedish men. Diabetes Care 28(7): 1805-1807.

32-Luo, W., Cao, Y., Liao, C. and Gao, F. (2012). Diabetes mellitus and the incidence and mortality of colorectal cancer: a meta-analysis of 24 cohort studies. Colorectal Disease 14(11): 1307-1312.

33-Boyle, T., Keegel, T., Bull, F., Heyworth, J. and Fritschi, L. (2012). Physical activity and risks of proximal and distal colon cancers: a systematic review and meta-analysis. Journal of the National Cancer Institute: 354.

34-Campbell, P. T., Patel, A. V., Newton, C. C., Jacobs, E. J. and Gapstur, S. M. (2013). Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. Journal of Clinical Oncology: JCO. 2012.2045. 9735.

35-Renehan, A. G., Tyson, M., Egger, M., Heller, R. F. and Zwahlen, M. (2008). Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. The Lancet 371(9612): 569-578.

36-Aleksandrova, K., Pischon, T., Buijsse, B., May, A. M., Peeters, P. H., Bueno-de-Mesquita, H. B., Jenab, M., Fedirko, V., Dahm, C. C. and Siersema, P. D. (2013). Adult weight change and risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition. European Journal of Cancer 49(16): 3526-3536.

37-Centers for Disease Control and Prevention (2013). Early Release of Selected Estimates Based on Data From the 2012 National Health Interview Survey. National Center for Health Statistics.

38-Cross, A. J., Ferrucci, L. M., Risch, A., Graubard, B. I., Ward, M. H., Park, Y., Hollenbeck, A. R., Schatzkin, A. and Sinha, R. (2010). A large prospective study of meat consumption and colorectal cancer risk: an investigation of potential mechanisms underlying this association. Cancer research 70(6): 2406-2414.

39-Secretan, B., Straif, K., Baan, R., Grosse, Y., El Ghissassi, F., Bouvard, V., Benbrahim-Tallaa, L., Guha, N., Freeman, C. and Galichet, L. (2009). A review of human carcinogens—Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. The lancet oncology 10(11): 1033-1034.

40-Liang, P. S., Chen, T. Y. and Giovannucci, E. (2009). Cigarette smoking and colorectal cancer incidence and mortality: Systematic review and meta-analysis. International journal of cancer 124(10): 2406-2415.

ISSN NO: 2770-2936
Date of Publication:11-12-2023

41-Ferrari, P., Jenab, M., Norat, T., Moskal, A., Slimani, N., Olsen, A., Tjønneland, A., Overvad, K., Jensen, M. K. and Boutron-Ruault, M. C. (2007). Lifetime and baseline alcohol intake and risk of colon and rectal cancers in the European prospective investigation into cancer and nutrition (EPIC). International journal of cancer 121(9): 2065-2072.

42-Cook, N. R., Lee, I.-M., Zhang, S. M., Moorthy, M. V. and Buring, J. E. (2013). Alternate-day, low-dose aspirin and cancer risk: long-term observational follow-up of a randomized trial. Annals of internal medicine 159(2): 77-85.

43-Murphy, G., Devesa, S. S., Cross, A. J., Inskip, P. D., McGlynn, K. A. and Cook, M. B. (2011). Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. International journal of cancer 128(7): 1668-1675.

44-Wong, R. J. (2010). Marked variations in proximal colon cancer survival by race/ethnicity within the United States. Journal of clinical gastroenterology 44(9): 625-630.

45-American Cancer Society. (2015). Cancer Facts and Figures. Atlanta, Ga: American Cancer Society. Inflamm Bowel Dis., 16:1097–1107.

46-Danesi, P. and Telleria, D. (2010). Radiological conditions at four selected sites in South Iraq with residues of depleted uranium. Proceedings of IRPA12: 12. Congress of the International Radiation Protection Association: Strengthening Radiation Protection Worldwide-Highlights, Global Perspective and Future Trends

47-Peterson, S. (1999). A special report—The trail of a bullet—Will America risk use of DU in Kosovo. DU‘s global spread spurs debate over effects on humans—A rare visit to Iraq‘s radioactive battlefield—DU‘s fallout in Iraq, Kuwait: a rise in illness

48-Little, J. B. (2000). Chapter 14: Ionizing Radiation. Cancer medicine, 6th edn. BC Decker, Hamilton

49-Greene, F. L., Page, D., Fleming, I., Fritz, A., Balch, C. and Haller, D. (2002). American Joint Committee on Cancer. AJCC cancer staging manual: xiv.

50-Schoen, R. E. (2000). Families at risk for colorectal cancer: risk assessment and genetic testing. Journal of clinical gastroenterology 31(2): 114-120.

51- Weisenberger, D. J., Siegmund, K. D., Campan, M., Young, J., Long, T. I., Faasse, M. A., Kang, G. H., Widschwendter, M., Weener, D. and Buchanan, D. (2006). CpG island methylator phenotype underlies sporadic microsatellite instability and is tightly associated with BRAF mutation in colorectal cancer. Nature genetics 38(7): 787-793.

52- Willis, A., Jung, E. J., Wakefield, T. and Chen, X. (2004). Mutant p53 exerts a dominant negative effect by preventing wild-type p53 from binding to the promoter of its target genes. Oncogene 23(13): 2330-2338.

ISSN NO: 2770-2936
Date of Publication:11-12-2023

53- He, X., Liao, J., Liu, F., Yan, J., Yan, J., Shang, H., Dou, Q., Chang, Y., Lin, J. and Song, Y. (2015). Functional repair of p53 mutation in colorectal cancer cells using trans-splicing. Oncotarget 6(4): 2034.
54- Olivier, M. and Taniere, P. (2011). Somatic mutations in cancer prognosis and prediction: lessons from TP53 and EGFR genes. Current opinion in oncology 23(1): 88-92.

55- Iacopetta, B., Russo, A., Bazan, V., Dardanoni, G., Gebbia, N., Soussi, T., Kerr, D., Elsaleh, H., Soong, R. and Kandioler, D. (2006). Functional categories of TP53 mutation in colorectal cancer: results of an International Collaborative Study. Annals of oncology 17(5): 842-847.