Study the role of thyroid hormones in colorectal cancer in Najaf / Iraq .

*MSc. Ezzate Hasson Ajeena

Department of Biology, Faculty of Sciences, Kufa University, Najaf, Iraq.

Corresponding Author: Email- ezath.abdulkarim@uokufa.edu.iq

Abstract

This study is designed to investigate the role of thyroid hormone in the incidence of colorectal cancer, besides to knowing the benefit of carcinoembryonic antigen tumor marker in detecting the prognosis of this disease.

This study involved 70 persons divided into two groups: control group which including thirty five healthy persons and malignant group which contain thirty five patients with colorectal cancer after excision the tumor and received chemotherapy. The results revealed that smoking habit and obesity which reflecting by Body mass index were significantly associated with increased risk of colorectal cancer incidence.

The result clarify a significant $P \leq 0.05$ decreasing in the levels of thyroid hormones (T3 and T4) in patients with colorectal cancer, reflecting that these hormones may suppress colorectal cancer invasiveness. Finally the statistical analysis of this study was explained that carcinoembryonic antigen (CEA) tumor marker significantly $P \leq 0.05$ increasing in patients in malignant group, referring to the importance of this tumor marker in follow up colorectal cancer patients for early diagnosis of recurrence.

1. Introduction

Cancer is the leading cause of death in economically developed countries and the second leading cause of the death in these countries[1]. Colon cancer is the

most commonly diagnosed cancer in Europe and one of the leading causes of cancer death worldwide [2]. Iraqi cancer registry recorded in 2008 about 693 case with colorectal cancer which divided in 378 case in male and 315 case in female and this type of cancer lie in the seventh degree in the commonest ten cancer in Iraq [3]. Colon cancer evolves via a sequence of alterations. In additional to the well-known adenoma-carcinoma sequence, some colorectal cancers are thought to arise from flat adenomas [4]

Colorectal cancer starts in the colon or the rectum. These cancers can also be referred to separately as colon cancer or rectal cancer, depending on where they start. Colon cancer and rectal cancer have many features in common. [5] In the past years treatment and outcome of early and advanced disease has steadily improved. Currently abroad variety of trail and retrospective analysis gave further insights into clinical questions like selection and duration of treatment [6].

No one knows the exact causes of colorectal cancer(CRC). Doctors often cannot explain why one person develops this disease and another does not. However, it is clear that colorectal cancer is not contagious. No one can catch this disease from another person. Research has shown that people with certain risk factors are more likely than others to develop colorectal cancer, such as(Age over 50 , Colorectal polyps, Family history of colorectal cancer, Ulcerative colitis or Crohn's disease) [7].

In addition to regulation of overall metabolism, thyroid hormones(TH) are important regulators of gut mucosal development and differentiation, inducing intestinal alkaline phosphatase (IAP). T3 has at least two major influences upon the adult small intestine; it is trophic for crypt cells and it alters the pattern of brush border enzyme expression in the villus enterocytes [8].

Given the important developmental and physiological functions of TH in the gut, a number of studies have examined the effects of TH on cancer prevention, development, and progression in various digestive tissues. Some of these relationships have been well characterized, while others remain poorly understood

[9]. In addition, major pathways in the development of CRC have been shown to be negatively regulated by thyroid hormone [10].

2.Materials and methods

2.1 Sampling of cases.

(a) Study group: thirty five cases of patients with colorectal cancer are included in this study, their ages ranging from 25 to 70 years. all of them were received chemotherapy treatment after malignant tumor excision.

(b) Control group: thirty five cases of normal human which were healthy and do not undergo any colon diseases or cardiovascular diseases or renal diseases and non-smoking .these cases were of the same age of malignant group.

The medical history of each patients was taken which include age, sex, family history, type of diet and smoking habit. measurements of height and weight were done to calculate body mass index.

2.2 Collection of blood samples .

Blood samples were collected from healthy control and malignant patients according to the method which used by [11].

2.3 Measurement of body mass index

Weight was measured to nearer 0.1 Kg and height was measured to nearer 0.5 cm by using the instrument for measurement of weight and height(DETECTOMEDIC). Body mass index(BMI) was calculated as follows:

$BMI=W/H^2$ W: Weight in kilogram , H^2: Height square in meter [12].

2.4 Measurement of hormones

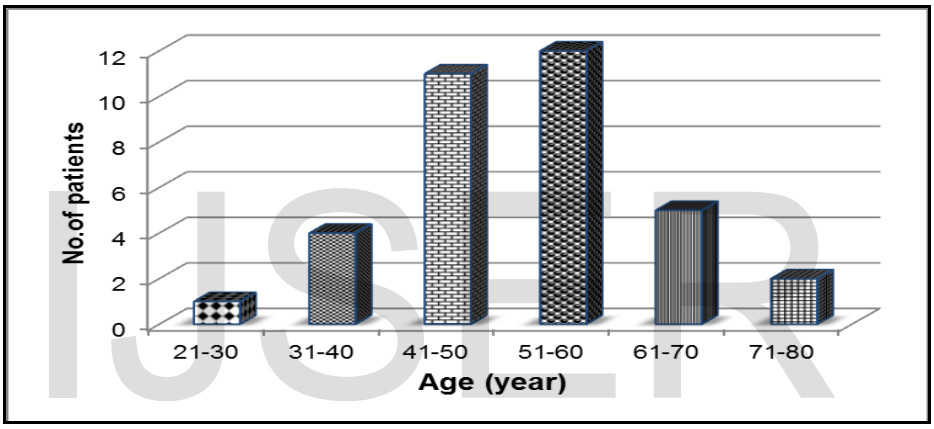
Reagents of triiodothyronine hormone (T3) and thyroxin hormone (T4) according toT3 and T4 hormones kits , Monobind, USA . Reagents of

carcinoembryonic antigen (CEA) tumor marker according to CEA kit, Human company, Germany.

3.Results

3.1 Age

The highest percentage of colorectal cancer patients under investigation was recorded in (51-60 years) with 12 cases followed by 11 cases were seen in (41-50 y), 5 cases in (61-70 y), 4 cases in (31-40 y), 2 cases in (71-80 y) while only one case was noted in (21-30 y). as shown in figure (1).



Figure(1): Distribution of age of colorectal cancer patients

3.2 Smoking

Table (1) clarifies that there was an increasing in the percentage of patients who smoke in malignant group 20(22.5%) as compared to people in control group which had no smoking habit. Malignant group showed a significant difference P≤0.05 when was compared with control group.

Table (1) Distribution of control and malignant groups according to smoking habit

Smoking	Control group		Malignant group		χ^2
	No .	%	No.	%	

Yes	0	0	20	22.5	**27.60[a]**
No	35	100	15	16.9	
Total	**35**	**100**	**35**	**100**	

a= significant differences when comparing malignant with control group at P<0.05**.**

3.3 Body mass index (BMI)

Table (2) shows that there was a highly significant difference P≤0.000 in the body mass index (BMI) among studied groups. Results of this table show that malignant group was characterized by increasing in the value of BMI (24.67**±**3.34) as compared with value of it in control group (20.10**±**1.66).

Table (2) Body mass index (BMI) (kg/m^2) in control and malignant groups .

Studied groups	No.	Mean±SD	P value
Control group	35	20.10**±**1.66	**0.000**
Malignant group	35	24.67**±3.34**	
Total	**70**	**22.38±3.49**	

3.4 Triiodothyronin hormone T3 .

The results of table (3) showed that the levels of T3 hormone significantly P<0.05 decreased in malignant group (0.86**±**0.31) as compared with control group (1.44**±**0.26).

Table (3) Serum T3 hormone levels (ng/ml) in control and malignant .

Studied groups	No.	Mean±SD	P value
Control group	35	1.44±0.26	**0.000**
Malignant group	35	0.86±0.31	

Total	**70**	**1.15±0.40**	

3.5 Tetraiodothyronin hormone T4

The results of table (4) were indicated that there was significantly decreasing P<0.05 in the level of T4 hormone in malignant group (7.58±1.50) as compared with control group (11.15±0.64).

Table (4) Serum T4 hormone levels (µg/dl) in control and malignant .

Studied groups	No.	Mean±SD	P value
Control group	35	11.15±0.64	**0.000**
Malignant group	35	7.58±1.50	
Total	**70**	**9.37±2.13**	

3.6 Carcinoembryonic antigen (CEA) tumor marker

Results in table (5) explain a highly significant difference P≤0.008 among studied groups in respect to the level of carcinoembryonic antigen CEA tumor marker. This table also shows that the level of this tumor marker in control group was (1.90±1.19) then this study recorded sharp elevation in the level of CEA tumor marker as noticed in malignant group (16.25±13.26).

Table (5) Serum CEA tumor marker levels (ng/ml) in control and malignant .

Studied groups	No.	Mean±SD	P value
Control group	35	1.90±1.19	**0.008**
Malignant group	35	16.25±13.26	

Total	**70**	**9.07±7.11**	

4. Discussion

In the present study maximum number of patients with malignant colorectal cancer were observed in (51-60 years) with 12 cases followed by 11 cases were seen in (41-50 y). These results agreed with [13] who explain that The incidence of colon cancer rises sharply with age, beginning at age 50 years . This phenomenon is attributed to accumulation of chance somatic mutations with age.

[14] in 2011 were explained in their study that there was increasing in the incidence of colorectal cancer in age group 55-59 years followed by the age group 65-69 years.

In this study ,there was a positive association of smoking with colorectal cancer risk and this study showed a significant difference $P \leq 0.05$ between malignant versus control groups the percentage of patients who habited to smoking in malignant group was (22.5%) compared with control group which recorded no woman with this habit .These findings were supported by [15], [16] in their studies which have shown the stronger association between cigarette smoking and risk of colorectal cancer, especially in relation to long term continuing smoking. [17] in 1996 hypothesized that carcinogens in cigarette smoke may act to initiate tumors in the colon and rectum, so that an induction period of 35–40 years may be needed to increase incidence.

Cigarette smoke contains more than 55 carcinogens, including polycyclic aromatic hydrocarbons (PAHs), heterocyclic aromatic amines, and N-nitrosamines [18]. There is already some direct evidence that tobacco carcinogens damage DNA in the human colonic epithelium. In one small study which done by [19] in 1996 has explain that DNA adducts to metabolites of benzo[*a*]pyrene, a potent PAH, were detected in colonic mucosa more frequently and at higher concentrations in smokers than in nonsmokers.

In the present study the results revealed a significant reduction in the levels of serum Triiodothyronin (T3) and Thyroxin (T4) hormones in malignant group in compared to control group, tables (3 and 4), these results were confirmed by [20] who reported that plasma T3 levels are found to be reduced in colorectal patients with systemic metastases, suggesting that thyroid hormones signaling may suppress colorectal cancer invasiveness.

[21] in 2006 that in addition to changes in thyroid hormones circulating levels, changes in expression of thyroid hormones receptors have been associated with colorectal cancer progression. In patient samples, colorectal tumors exhibit reduced expression of thyroid receptor TRβ1 compared to matched normal mucosa. TRβ1 expression is associated with a more differentiated phenotype .

This study also showed that there was significantly increased in the levels of Carcinoembryonic antigen CEA tumor marker in malignant group compared with control group (table 5), this result means that the recurrence rate was higher in those who had elevated CEA levels irrespective of their stage[22].

[23] in 1994 referred that there was usefulness of postoperative CEA monitoring for early detection of recurrence after curative surgery and for assessment of response to chemotherapy in metastatic colorectal cancer.

[24] have shown a shorter disease free survival (DFS) and overall survival (OS) in patients with high value of CEA tumor marker ,this means that this marker is independent prognostic factor for both DFS and OS [25].

5. conclusion

This study concluded the following:(1) Colorectal cancer was found to be spread in patients with the age of fifties and sixties of age.(2) The role of smoking and obesity as important risk factors contributing in the increase of the incidence of colorectal cancer .(3) Thyroid hormones play anticancer role in patients with colorectal cancer.

6. References

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