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Colorectal Cancer in Patients with Thyroid Dysfunction

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Abstract

Background: Colorectal cancer (CRC) is one of the most serious diseases diagnosed globally. A few research have been conducted to explore the effect of thyroid dysfunction on the progression and danger of CRC. This study aimed to evaluate the prevalence of colorectal carcinoma in individuals who have thyroid disorders.

Patients and methods: This was a case–control study with 60 persons, who were divided into three groups: Group (I) contained 20 hyperthyroid patients, Group (II) involved 20 hypothyroid patients, and Group (III) included 20 patients with normal thyroid function (control group).

Results: When compared with groups (I) and (III), group (II) had an extremely statistically significant increase in TSH (P value 0.001). (III). When compared with groups (I) and (III), there was a highly statistically significant rise in serum carcinoembryonic antigen (CEA) in groups (II) and (III). In comparison to groups (II) and (III), there was a highly statistically significant rise in CA 19–9 in group (III) and (I). Compared with groups (III) and (IV), there was a highly statistically significant increase in carbohydrate antigen 125 (CA 125) in groups (II) and (I). In neither of the groups examined did anyone have an abnormally high CA 125 level. The rate of occurrence of colorectal cancer was not significantly different across the groups.

Conclusion: Consistent with the results of the current investigation, both hyperthyroidism and hypothyroidism were associated with a reduced risk of developing CRC.

Keywords: Colorectal cancer, Hyperthyroidism, Hypothyroidism, Thyroid dysfunction

1. Background

CRC, which involves colon and/or rectal cancer, is a major public health issue because it is the third most common and second most potentially lethal cancer worldwide.¹

The large percentage of CRC is infrequent and is caused mainly by a constellation of changing risk factors associated with westernization (for example, overweight, lack of physical activity, poor diets, consumption of alcohol, and smoking).²

Thyroid hormone (TH) levels have been connected to cancer since 1896 when Beatson used

thyroid extract as a possible treatment for breast carcinoma.³

Thyroid hormones not only govern normal cell physiological processes, but they also promote cancer cell proliferation.⁴ Although numerous studies have been made, few studies have investigated the involvement of thyroid issues in the development and risk of CRC, despite the fact that it is known that thyroid dysfunction is connected with an enhanced danger of pancreatic and breast cancer.⁵

The purpose of this research was to determine how common colorectal cancer is among people whose thyroids are not working properly.

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2. Patients and methods

This investigation focused on 60 individuals. The participants were split into three groups: group (1) composed of 20 patients with hyperthyroidism, group (2) composed of 20 patients with hypothyroidism, and group (3) composed of 20 patients with normal thyroid function (control group).

2.1. Inclusion criteria

Age >18 years.

Patients with hypothyroidism.

Patients with hyperthyroidism.

Patients under the age of 18 years were disqualified; had extra colonic malignancy; had colorectal cancer before the index date; if pregnant and had a family history of CRC.

The following tests were done: Aspartate aminotransferase and alanine aminotransferase gamma-glutamyl transferase, and total bilirubin were measured on an automated biochemistry analyzer. (ADVIA Chemistry XPT System) Siemens Healthcare Diagnostics Products GmbH. U.S.A. Distributor. Siemens Healthcare Diagnostics Inc. Newark, DE 19714 U S A. www.siemens.com/diagnostics. Estimation of serum creatinine (Linear Chemicals, SLU Joaquim Costa 18 2^a planta. 08390 Montgat (Barcelona) Spain). Uric acid was measured using the calorimetric method: To generate a quantifiable change of color, a colorimetric process based on the decrease of a chromogen, like sodium tungstate, by uric acid was used. Apart from urate, the technique estimates ascorbic acid and other substances. Colorimetric assessments are usually believed to overestimate true uric acid levels, with the typical levels being 1 mg/dl > than the more specific enzymatic methods.⁶ Electrochemiluminescence immunoassay (ECLIA) was used to measure free thyroxine (FT4) and thyroid-stimulating hormone (TSH) in -70 °C stored serum samples utilizing Roche Diagnostics packs and a Roche/Hitachi Cobas

e-411 analysis software (GmbH, Mannheim, Germany). CEA ELISA: (Diagnostic Automation, INC. 23961 Craftsman Road, Suite D/E/F, Calabasas, CA 91302). The CA19-9 EIA test: (Diagnostic Automation, INC. 23961 Craftsman Road, Suite D/E/F, Calabasas, CA 91302). The CA125 ELISA test: (Panomics, Inc. 6519 Dumbarton Circle, Fremont CA 94555 1-877-726-6642). Thyroid ultrasonography, pelvic and abdominal US, colonoscopy, and biopsy were done.

2.2. Statistical evaluation

Using SPSS 24, a statistical program for social scientists, the data was evaluated. Mean and standard deviation were used to summarize the data. The frequency and proportion of qualitative data were used. The mean (average) of a separate collection of numbers is the total amount of the values split by the number of values. The standard deviation (SD) of a collection of values is an assessment of its distribution. A low SD suggests that the values are near the set's mean, whereas a high SD implies that the values are spread out over a larger scope. The next evaluations were carried out: Kruskal–Wallis test (KW) was used when equating >2 means (for abnormally distributed data). ANOVA (F) should be used when comparing >2 means (for normally distributed data). When comparing nonparametric data, the Chi-square test was used. Post hoc test was used to create numerous comparisons among variables. Probability (*P* value): *P* values of <0.05 were found to be significant; *P* values of <0.001 were regarded as highly significant; and *P* values > 0.05 were regarded insignificant.

3. Results

The following tables and figures show the findings of the current study [Tables 1–4](#), [Fig. 1](#).

Table 1. Comparisons among the patient groups regarding age and gender.

		Groups						Stat. test	P-value
		Group I (n = 20)		Group II (n = 20)		Group III (n = 20)			
Sex	Male	11	55%	8	40%	12	60%	X ² = 1.7	0.420 NS
	Female	9	45%	12	60%	8	40%		
Age(years)	Mean	55.3		56.2		51.5		F = 1.5	0.214 NS
	±SD	9.4		7.6		9.5			

F, F value of ANOVA test; NS, *P* value > 0.05 is considered nonsignificant; X², Chi-square test.

Table 2. Comparisons between the patient groups regarding laboratory data.

		Groups			Stat. test	P-value
		Group I (n = 20)	Group II (n = 20)	Group III (n = 20)		
Hb(g/dl)	Mean	14.01	13.1	12.7	F = 2.29	0.111 NS
	±SD	1.6	1.9	1.9		
PLTs($\times 10^9/\mu\text{l}$)	Mean	216.6	217.9	324.5	F = 27.3	< 0.001 HS
	±SD	13.8	23.1	87.7		
INR	Mean	1.06	1.15	1.08	KW = 2.89	0.235 NS
	±SD	0.11	0.17	0.12		
ALB(g/dl)	Mean	4.2	3.8	4.5	KW = 24.5	< 0.001 HS
	±SD	0.5	0.3	0.3		
T. bilirubin(mg/dl)	Mean	0.7	0.8	0.8	F = 0.073	0.930 NS
	±SD	0.3	0.4	0.2		
AST(U/L)	Mean	26.2	25.9	26.7	F = 0.11	0.894 NS
	±SD	4.6	5.7	5.8		
ALT(U/L)	Mean	28.1	28.0	25.2	F = 1.88	0.161 NS
	±SD	5.7	5.6	5.0		
Creat(mg/dl)	Mean	0.9	0.8	1.0	KW = 5.4	0.066 NS
	±SD	0.2	0.2	0.6		
TSH($\mu\text{IU/ml}$)	Mean	0.2	5.0	2.6	KW = 53.4	< 0.001 HS
	±SD	0.04	0.8	0.4		
T3(ng/ml)	Mean	1.6	1.0	0.7	KW = 47.8	< 0.001 HS
	±SD	0.3	0.2	0.1		
T4($\mu\text{g/dl}$)	Mean	12.0	1.2	7.2	F = 307.1	< 0.001 HS
	±SD	2.1	0.2	1.2		

Table 3. Comparisons among studied groups as regards studied tumor markers.

		Groups			Stat. test	P-value
		Group I (n = 20)	Group II (n = 20)	Group III (n = 20)		
CEA(U/ml)	Mean	0.9	1.2	0.8	KW = 25.8	< 0.001 HS
	±SD	0.5	0.5	0.1		
CA 19-9(U/ml)	Mean	9.3	10.3	12.6	KW = 17.1	< 0.001 HS
	±SD	1.8	2.1	2.5		
CA 125(U/ml)	Mean	5.6	8.1	7.6	F = 29	< 0.001 HS
	±SD	0.8	1.7	1.1		

Table 4. Comparisons among studied groups as regards incidence of colorectal cancer.

		Groups				Stat. test	P-value		
		Group I (n = 20)		Group II (n = 20)				Group III (n = 20)	
Colo-rectal cancer	No	19	95%	19	95%	20	100%	X ² = 1.03	0.596 NS
	Yes	1	5%	1	5%	0	0%		

NS: P-value > 0.05 is considered non-significant.

X²: Chi-square test.

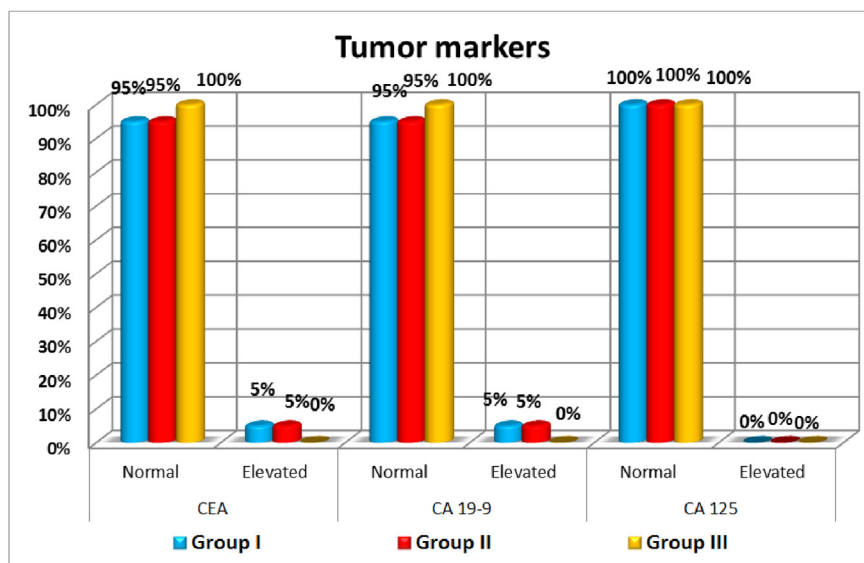


Fig. 1. Comparisons between the patient groups regarding the studied tumor markers.

4. Discussion

The present study results showed male predominance in group (I); 55% were men and 45% were women. Despite the group's gender balance favoring women (II), 40% were men and 60% were women. In group (III), 60% were males and 40% were females. There was no statistically significant difference between the studied groups regarding gender (P value = 0.420).

These results agreed with Unnikrishnan *et al.*⁷; the female gender was discovered to have a significant relationship with hypothyroidism. In the study of Unnikrishnan *et al.*,⁷ females had a significantly higher overall incidence of hypothyroidism and hyperthyroidism than males.

The mean age of the patients in the study groups was (55.3 ± 9.4) in group (I), (56.2 ± 7.6) in group (II), while it was (51.5 ± 9.5) in group (III). These results disagreed with a previous study of L'Heureux *et al.*⁸ The participants' average age was (65.9 ± 13.7).

The findings of this study revealed a highly significant rise in platelet count ($P < 0.001$) in group (III) (324.5 ± 87.7) compared with group (I) (216.6 ± 13.8) and group (II) (217.9 ± 23.1).

Hypothyroidism and hyperthyroidism are the most prevalent endocrine dysfunctions that impact blood cells and cause thrombocytopenia.⁹ Platelets have also been linked to the development and progression of malignancies.¹⁰ Dymicka-Piekarska *et al.*¹¹ findings showed that platelet activation occurs regardless of the clinical stage of colorectal cancer.

Our study results showed a highly statistically significant decrease in ALB (P value < 0.001) in

group (II) (3.8 ± 0.3) when compared with group (I) (4.2 ± 0.5) and group (III) (4.5 ± 0.3).

The relationship between serum albumin and thyroid profile was also investigated in the Muralleedharan and Beegum¹² study; TSH and serum albumin were discovered to have a negative correlation. Our results match with the study of Li *et al.*¹³ who found that serum albumin amounts were reduced in hypothyroidism and reduced T3/T4 groups than in the ordinary thyroid function group.

The present study's findings revealed a statistically significant rise in TSH in group (II) (5 ± 0.8) when compared with groups (I) (0.2 ± 0.04) and group (III) (2.6 ± 0.4).

TSH is the most accurate indicator of thyroid function.¹⁴ Similarly, a significant proportion (28%) of subjects who self-reported being hypothyroid still had a high TSH value in the findings of Unnikrishnan *et al.*⁷

Our study results showed a highly statistically significant increase in free triiodothyronine (T3) (P value < 0.001) in group (I) (1.6 ± 0.3) when compared with group (II) (1.0 ± 0.2) and group (III) (0.7 ± 0.1). Also, there was a highly statistically significant increase in serum thyroxine (T4) in group (I) (12 ± 2.1) when compared with group (II) (1.2 ± 0.2) and group (III) (7.2 ± 1.2).

Similar to our findings, in Graves' hyperthyroidism, the intrathyroidal deiodination of T4–T3 increases.¹⁵ Hyperthyroidism is a pathological condition associated with higher free (T4) and/or total (T4) thyroid hormone levels (T3).¹⁶

Regarding results of tumor markers in the present work, there was a highly statistically significant rise

in serum carcinoembryonic antigen (CEA) in group (II) (1.2 ± 0.5) when compared with group (I) (0.9 ± 0.5) and group (III) (0.8 ± 0.1). There was one patient (5%) in group (I) and group (II) with elevated CEA; in the meantime, there were no patients (0%) with elevated CEA in group (III).

Similar findings were obtained by *Amino et al.*,¹⁷ who found that people who had hypothyroid with Hashimoto's disease recorded a significantly higher incidence of CEA positivity and that hormone replacement therapy lowered CEA thresholds in hypothyroid patients. Tumor marker rise is believed to be caused by increased expression or lowered metabolism overall. Hypothyroidism may influence CEA metabolic activity or clearing by the hepatocytes, as CEA is metabolized and excreted by the liver.¹⁸ Also, *Kawaguchi et al.*¹⁹ reported a case of high CEA levels in a patient with hypothyroidism. Also our results agreed with *Hashimoto & Matsubara*,²⁰ who found that patients with hypothyroidism had significantly elevated mean CEA levels compared with those with normal and hyperthyroidism.

A statistically considerable increase occurred in CA 19–9 in group (III) (12.6 ± 2.5) when compared with group (II) (10.3 ± 2.1) and group (I) (9.3 ± 1.8). There was one patient in group (I) and group (II) with elevated CA 19–9, while there were no patients (0%) with elevated CA 19–9 in group (III).

The level of CA 19–9 was higher in the control group in the present study. Similarly, the *Kim et al.*²¹ study highlighted the common benign disorders responsible for CA 19–9 elevation. In a hypothyroid patient, the CA 19-9 amount was raised while the CEA was not raised.²²

There was highly statistically significant increase in carbohydrate antigen 125 (CA 125) in group (II) (8.1 ± 1.7) when compared with group (III) (7.6 ± 1.1) and group (I) (5.6 ± 0.8). There were no patients with elevated CA 125 in all studied groups.

There are few findings of transitory elevations of serum biomarkers in hypothyroidism. Similarly, in *Takahashi et al.*²³ study, the case of hypothyroidism showed markedly elevated concentrations of CEA and CA 125. In another condition, an elderly female with considerable hypothyroidism, serious ascites, and a CA 125 concentration of 684 U/ml had become euthyroid, and her ascites cleared up and her CA 125 concentration levels went back to normal.²⁴

The present study identified no statistically significant variation (P value = 0.596) in colorectal cancer rates among study subjects. Colorectal cancer occurred in 5% of group (I) and 5% of group (II) and (II).

In agreement with our results, both hyperthyroidism and hypothyroidism were found to be linked to a lower threat of CRC identification in the study of *L'Heureux et al.*⁸ In contrast, according to *Boursi et al.*,²⁵ there was an elevated risk of colorectal cancer in those with hyperthyroidism or untreated hypothyroidism.

A single population-based prospective research *Hellevik et al.*²⁶ discovered a link between hyperthyroidism and a higher likelihood of CRC; however, the increase was not statistically significant due to the small cohort size.

TR1 and TR1 were also two extranuclear receptors that have antagonistic impacts on colorectal cancer. The impact of thyroid hormones on TR1 activates catenin, resulting in cellular proliferation in the colon. TR1 prevents cellular proliferation once energized by thyroid hormones. As a result, an absence of TR1 affirmation in colon cancer has been connected to cancer development.²⁷

4.1. Conclusion

The chance of having CRC is reduced in those with either hyperthyroidism or hypothyroidism.

Disclosure

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Authorship

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Conflicts of interest

The authors declared that there were no conflicts of interest.

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