Hormozgan Medical Journal

doi 10.5812/hmj.102085

Hormozgan Med J. 2021; 25(1):9-13

Research Article

Serum Lipid Profile and Steroid Hormone Levels in Patients With Colorectal Cancer

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Abstract

Background: Lipids are usually crucial to develop tumors, and dyslipidemia is correlated with the high chance of colon and colorectal cancer (CRC). Steroid hormones such as estrogen and progesterone can decrease the risk of CRC development.

Objectives: The present study aimed to compare the serum levels of lipid profile and steroid hormones in patients with CRC and healthy controls.

Methods: The present study included 40 consecutive adult patients with CRC in the Mazandaran Cancer Center, Sari, Iran, between 2017 and 2020. The diagnosis of CRC was evaluated based on colonoscopy with biopsy and CT scan. Also, the diagnosis of CRC was based on NCCN clinical practice guidelines in oncology. Blood samples were taken before treatment during routine testing. A 5 mL of peripheral blood was collected from each patient. All patients signed the written consent for the study. Also, a total of 40 healthy subjects were selected as healthy controls from the same area during a routine physical examination, which was also confirmed by screening colonoscopy and pathology. Serum total cholesterol (TCH) and triglyceride (TG) levels were quantitatively determined by the colorimetric method. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were determined by the turbidimetric immunoassay. Steroid hormones were quantitatively determined by the enzyme-linked immunosorbent assay (ELISA) according to the reagent manufacturer's instruction. To analyze data, the SPSS software package (version 21) was applied.

Results: Among all the indicators studied, the mean ± SD of testosterone, follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels was higher (1.85 ± 1.63 ng/mL, 15.35±0.13 mIU/L, 12.42±0.12.16 mIU/mL) in patients with CRC than healthy controls (0.40±.0.21 ng/mL, 6.27±0.50 mIU/mL, 2.89±0.20 mIU/mL, $P<0.05$ respectively). The results in subgroups showed that the mean testosterone (0.91±1.2 ng/L), FSH (19.11±16 mIU/mL) , LH (14.49±14 mIU/mL) levels in the female patients with CRC was higher than healthy female controls and had more statistical significance($P=0.02$, 0.00, 0.00), respectively. The area under the AUC cure of the testosterone, FSH, and LH indicates positive test (0.670, 0.726 and 0.775).

Conclusion: Changes in the levels of steroid hormones and lipids could correlate with the elevated chance of CRC. Therefore, assessment of multiple markers might overcome and provide better judgment in patients with CRC.

Keywords: Colorectal cancer, DHEA, lipid profile, HDL-C, LDL-C, TG, Steroid hormones, Estradiol, Testosterone

Received April 12, 2020, **Accepted:** August 3, 2020, **Published Online:** November 10, 2020

Background

Colorectal cancer (CRC) the third most common cancer in the world, is a common malignancy with poor prognosis and survival rates. It is one of the leading causes of cancer-related deaths worldwide (1). CRC has originated from the epithelial cells lining the colon or rectum of the gastrointestinal tract. Symptoms of CRC include blood in the stool, change in bowel movements, weight loss, and feeling tired. It might be caused by old age, lifestyle, and genetic disorders. CRC was diagnosed by the sampling of areas of the colon suspicious for possible tumor development. CRC is the most common cancer in Iranian population and ranks third in Iranian men and fourth in women. (2). In this regard, lipoproteins are vital in cancer progression by providing lipids for malignant cells and tumors (3). Although several studies have been conducted on the relationship between serum lipids, plasma lipoproteins, and cancers, there is little research on the association between blood lipids profile, colon, and CRC (4,5). Changes in serum cholesterol

levels in the CRC diagnosis process have been observed (6). On the other hand, the levels of total cholesterol (TCH) and low-density lipoprotein cholesterol (LDL-C) and the LDL-C/high-density lipoprotein cholesterol (HDL-C) ratio were significantly higher in patients with CRC than controls (7). Furthermore, dyslipidemia was correlated with the elevated chance of colon and CRC, but the results regarding the increase, decrease or inactivity of fats are inconsistent and still controversial. Also, the role of steroid hormones, especially testosterone, has increased the risk of CRC (8). Epidemiological studies have shown that an increase in female sex hormones such as estrogen and progesterone can decrease the risk of CRC development. On the other hand, women are less likely to suffer from CRC than men due to the protection role of the estrogens (9). Studies have interestingly shown that testosterone hormone has a stronger effect in developing CRC than the protecting effect of estrogen hormone. Also, after the decrease of testosterone, the rate of incidence of CRC can be decreased (10). Estrogen supplementation in postmenopausal females can enhance HDL-C (11). Also, it reduces the total and LDL-C concentration in women (12). According to the researchers, estrogen provokes the LDL-C degradation and decreases the assembled LDL particles oxidation in the endothelium (13). Besides, the hormones, lipids, the expression of genes, proteins, and some biomarkers released by tumors suggested as vital to develop some cancers, and they may play a role in the detection of cancers (14-18). Therefore, the assessment of multiple markers might overcome and provide better judgment in patients with CRC. In this regard, this research aimed to investigate the altered serum levels of lipid profile and steroid hormones in patients with CRC and test the hypothesis that serum levels of lipid profile and steroid hormones may affect the CRC patients.

Objectives

The objective of this study was to compare the serum levels of lipid profile and steroid hormones in patients with CRC and healthy controls**.**

Methods

A total of 40 CRC patients were consecutively recruited from the hospitalized in the Imam Khomeini educational hospital and Tuba clinic, Mazandaran University of Medical Sciences, in Sari between January 2017 and April 2020. The patients were within the age range of 30 to 70 years (20 males and 20 females). The diagnosis of CRC was based on NCCN clinical practice guidelines in oncology (19). The patients had no medications before the sample collection. Having consulted with a gastroenterologist, we verified the diagnosis of the patients. All patients with biopsy-proven CRC were included in the study. The International Classification of Diseases was used to identify patients with a diagnosis of CRC, and diagnoses were verified from a registry kept by the pathology department. Demographic data, including name, age, gender, and race, were collected. In this study, Also, a total of40 (8 males and 32 females), aged 30–70 years old were selected as healthy controls from the same area during a routine physical examination, which was also confirmed by screening colonoscopy and pathology. The control group was healthy volunteers who were not taking medicine or any form of hormonal medication and were matched to cases by study center, sex, age time of blood collection, and fasting status. Venous blood samples were collected after an overnight fast from the patients. The blood was allowed to clot, centrifuged at 3000 rpm for 10 minutes, and serum was collected and stored at -80oC until assayed. Written informed consent was taken from all patients as well as healthy controls.

Serum TCH and triglyceride (TG) levels were quantitatively determined by the colorimetric method called a Roche Mindray- BS-800 Automatic Biochemistry Analyzer. LDL-C and HDL-C were determined by the turbidimetric immunoassay (20). Steroid hormones were quantitatively determined by the Enzyme-linked immunosorbent assay (ELISA) according to the reagent manufacturer's instruction. The selection criteria were patients with a confirmed diagnosis of CRC who were 30-70 years of both sex and who resided in the Mazandaran. Participants were selected based on the information obtained by clinical records (Testosterone Elisa Kit, Ideal Tashkhis Atieh, Iran; Cat. No: 2424-96, Estradiol E2 Elisa Kit, Ideal Tashkhis Atieh, Iran; Cat. No: 2824-96, DHEA-S Elisa Kit, Ideal Tashkhis Atieh, Iran; Cat. No: 2624-96, FSH Elisa Kit Ideal Tashkhis Atieh, Iran; H03LIG8. LH Elisa Kit, Ideal Tashkhis Atieh, Iran; H02LIH8. Triglycerides diagnostic Kit, GPO-PAP, Pars Azmun. Cholesterol diagnostic Kit, CHOD, Pars Azmun. LDL-C diagnostic Kit Pars Azmun. HDL-C diagnostic Kit Pars Azmun).

Statistical Analysis

We used the SPSS software package (version 21) to analyze the data. The results were expressed as means ± standard deviations (SD). We also used *t* tests to compare the CRC patients and control groups in terms of the lipid profile and steroid hormone levels. A *P*-value <0.05 was set to be statistically, significant. The receiver operating characteristic (ROC) was conducted for testosterone, FSH, and LH. Pearson rank correlations were used to run the correlation analysis between quantitative variables.

Results

Table 1 summarizes the demographic characteristics of all subjects enrolled in the study. The mean age of patients with CRC was 60 ± 9.42 years (range 30–70 years); eligible patients had histologically or pathological tests. The mean age of healthy controls was 43 ± 13.4 years (range 30–70 years). Serum steroid hormones and lipid profile levels in patients with CRC and healthy controls are shown in Tables 2 and 3, respectively. The mean of testosterone,

Table 1. Demographic Features of CRC Patients and Healthy Controls

	Control Group	Cancer Group	*P* Value
Number	40	40	
Gender			0.005
Female	32	20	
Male	8	20	
Age, year (mean ± SD)	43 ± 13.4	60 ± 9.42	0.059
Weight (kg) (mean ± SD)	69.38±8.16	73.32±11.63	0.048
BMI (kg/m^2) (mean ± SD)	25.61±2.31	27.22±4.3	0.001

[a] *P* values for case–control comparisons from chi-square and *t* test.

FSH, and LH levels (1.85 ± 1.63 ng/mL, 15.35±0.13 mIU/L, 12.42±0.12.16 mIU/mL) were significantly higher in patients with CRC, in healthy controls (0.40±.0.21 ng/mL, 6.27±0.50 mIU/mL, 2.89±0.20 mIU/mL (Table 2). Also, the results in sub-groups showed that the mean testosterone (0.91±1.2 ng/L), FSH (19.11±16 mIU/mL), LH (14.49 ± 14 mIU/mL) levels in the female patients was significantly higher than healthy controls. The area under the AUC cure (Figure 1) of the testosterone, FSH, and LH indicates a positive test (0.670, 0.726, and 0.775, respectively). Table 4 shows the relationship between hormones and lipids levels in patients with CRC.

Discussion

According to this study, the levels of FSH, LH, DHEA, and testosterone in female patients with CRC increased significantly when compared to healthy controls. However, their level of estradiol was decreased. Based on the results, male patients with CRC showed a statistically significant increase in the levels of FSH, LH, and estradiol, although, unlike healthy control, their level of DHEA and testosterone was decreased. The present study also showed that the level of TG in female patients with CRC, unlike healthy control, was decreased. In male patients with CRC, there was an increase in the level of TCH, HDL-C, and LDL-C, compared to healthy control. These results showed the importance of lipid and lipoproteins in CRC, which is in line with the fact that lipids are usually crucial to develop tumors, and lipoproteins have shown critical for cancer progression (3). The results also showed the association between lipids profile and colon and CRC rates (4, 5). Moreover, reductions in serum

Table 2. Mean Values of the Studied Steroid Hormone Levels in CRC Patients and Control Group

Variables	group	Total			Men			Woman		
		N	Mean ± SD	*P* Values[a]	N	Mean ± SD	*P* Values[a]	N	Mean ± SD	*P* Values[a]
1-Testosterone	CRC	38	1.48±1.63	0.00	19	2.05±1.81	0.23	19	0.91±1.2	0.02
	Control	33	0.40±.0.21		2	0.46±0.11		31	0.40±0.21	
DHEA	CRC	37	0.75±.0.49	0.64	20	0.66±0.54	0.05	17	0.86±0.41	0.56
	Control	39	0.83±0.79		8	1.15±0.66		31	0.74±0.81	
Estradiol	CRC	37	41.73±0.21	0.28	20	43.45±17	0.78	17	39.71±0.25	0.31
	Control	36	48.55±0.31		8	45.74±24		28	49.36±0.33	
FSH	CRC	37	15.35±0.13	0.00	20	12.15±9	0.38	17	19.11±16	0.00
	Control	35	6.27±0.50		8	8.92±4		27	5.48±6	
LH	CRC	39	12.42±0.12	0.00	20	10.46±11.01	0.06	19	14.49±14	0.00
	Control	34	2.89±0.20		8	2.01±1.72		26	2.89±2.5	

Abbreviations: CRC, colorectal cancer; DHEA, dehydroepiandrosterone; FSH, follicle-stimulating hormone; LH; luteinizing hormone.
[a] *P* values for case–control comparisons from *t* test.

Table 3. Mean Values of the Studied Lipid Profile Levels in CRC Patients and Control Group

Variables	Group	Total			Men			Woman		
		N	Mean ± SD	*P* Values[a]	N	Mean ± SD	*P* Values[a]	N	Mean ± SD	*P* Values[a]
TCH	CRC	39	179.79±53	0.934	19	180.52±51	0.490	20	179.1**±56**	0.811
	Control	38	178.89±40		8	165.87±44		30	182.3**±39**	
TG	CRC	37	153.13±177	0.584	18	181.44±253	0.865	19	126.3**±26**	0.037
	Control	38	170.68±84		8	165.62±61		30	172.03**±90**	
LDL	CRC	40	108.55±39	0.566	20	107.75±39	0.532	20	109.35**±40**	0.704
	Control	39	104.10±27		8	97.75±32		31	105.74**±26**	
HDL	CRC	40	45.72±14	0.179	20	47.18±15	0.057	20	44.27**±13**	0.734
	Control	39	41.15±15.		8	34.78±13		31	42.80**±15**	

Abbreviations: CRC, colorectal cancer; TCH, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein.
[a] *P* values for case–control comparisons from *t* test.

Table 4. Relationship Between Hormone Levels and Lipid Levels in Patients With CRC

		Testosterone	DHEA	Estradiol	FSH	LH
TCH	Pearson correlation	0.083	-0.063	-0.115	0.217	-0.042
	Sig. (2-tailed)	0.500	0.599	0.343	0.072	0.726
	N	69	73	70	70	71
TG	Pearson correlation	0.034	-0.026	-0.003	-0.042	-0.102
	Sig. (2-tailed)	0.783	0.827	0.978	0.737	0.410
	N	67	71	68	67	68
LDL	Pearson correlation	0.072	-0.049	-0.084	0.190	0.014
	Sig. (2-tailed)	0.551	0.679	0.486	0.110	0.909
	N	70	75	72	72	73
HDL	Pearson correlation	0.168	0.002	-0.098	0.156	-0.009
	Sig. (2-tailed)	0.165	0.987	0.414	0.191	0.942
	N	70	75	72	72	73

Abbreviations: CRC, colorectal cancer; DHEA, dehydroepiandrosterone; FSH, follicle-stimulating hormone; LH; luteinizing hormone; TCH, total cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

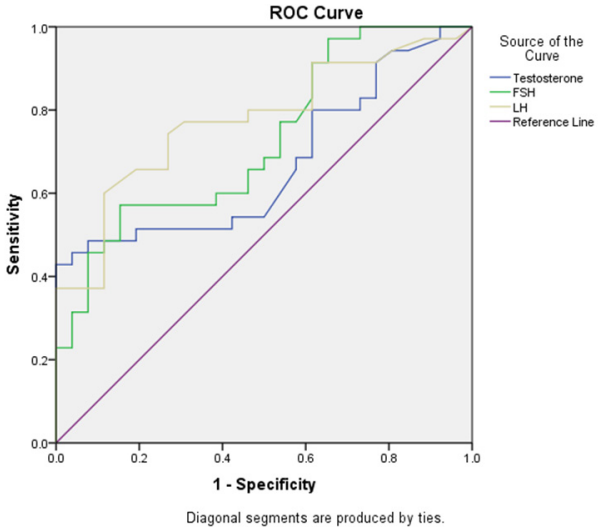

Figure 1. Analysis of TESTOSTERONE, FSH, and LH of Sensitivity and Specificity in the Diagnosis of CRC by ROC Curve. Data from the spectrophotometric method for FSH and LH (Considering the larger test result indicates more positive test). ROC curve analysis shows area under receiver operating characteristic (AUROC) 0.670, 0.726, and 0.775. AUROC > 0.9; high accuracy, AUROC = (0.7-0.9); moderate accuracy, AUROC = (0.5-0.7); low accuracy.

cholesterol levels were observed in patients with CRC (6). It was reported that the levels of TCH and LDL-C and the LDL-C/HDL-C were significantly higher in patients with CRC than healthy controls (7). Also, the role of steroid hormones, such as testosterone, was to increase the risk of CRC (8). Increasing female sex hormones such as estrogen and progesterone can decrease the risk of CRC development due to the protection roles of these hormones (9). Besides, our results showed that testosterone and DHEA level are high in CRC female patients, but the estradiol level is low. Thus, testosterone and DHEA hormone have a stronger effect in developing the process of CRC than the protecting effect of estradiol.

Our findings confirmed the findings of other investigators (10). Our results showed that in CRC male patients the levels of HDL-C, LDL-C, TG, and TCH are high, compared to healthy controls, which was not confirmed in the findings of other investigators (11) because they used different study designs, had different populations, investigated different sample types, and utilized a variety of analytical methods to measure hormones (12). It is well known that estrogen supplementation can reduce the total and LDL- cholesterol concentration in women (12). Estrogen provokes the degradation of LDL cholesterol (13). Further, ROC curve analysis confirmed that serum testosterone, LH and FSH act as discriminatory factors to differentiate CRC patients from healthy controls. Therefore, serum testosterone, LH, and FSH could be used as markers to diagnose and monitor CRC and obtain positive outcomes in therapy. However, challenges remain for using lipid profile and steroid hormones as biomarkers in CRC and need to do more investigations.

Authors' Contribution

DQ and RH designed the experiments; RA and VH performed the experiments; RA analyzed the results and wrote the manuscript.

Conflict of interests

The authors declare that they have no conflict of interests.

Ethical Approval

All protocols involving patients and control subjects were confirmed by the Ethics Committee of Payame Noor University with the code number of (IR.PNU.REC.1397.036). Written informed consent was obtained from all participants before enrollment.

Funding/Support

This study was supported by Department of Biochemistry, Faculty of Sciences, Payame Noor University, Tehran, Iran (No: 2 - 1396/10/26) as PhD thesis.

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