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Comparison of the Serum Total Bile Acids and Cholesterol Levels in Breast Cancer Patients with Control Group

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ABSTRACT

BACKGROUND AND OBJECTIVE: Identification of breast cancer risk factors is very important. Cholesterol by acting on tumor cells is considered as one of the risk factors for breast cancer. The conversion of cholesterol to bile acids is one of the major mechanisms of cholesterol excretion from body. In this study, total bile acids and cholesterol concentrations were evaluated in breast cancer patients.

METHODS: In this case-control study, 109 of patients who breast cancer was confirmed by pathological examination and 109 healthy subjects who had normal physical exam and negative mammograms to rule out breast cancer were studied. Fasting serum total bile acids and cholesterol levels were measured enzymatically and then the data were analyzed.

FINDINGS: The mean of total bile acids in breast cancer patients and control group were 11.67±0.92 and 13.36±0.81 µmol/l, respectively ($p<0.05$). Mean of cholesterol levels in breast cancer patients was 316.98±15.35 mg/dl and control group was 212.08±5.79 mg/dl ($p<0.001$).

CONCLUSION: According to the results, lower amounts of body cholesterol are converted to bile acids in breast cancer patients.

KEY WORDS: *Breast Cancer, Total Bile Acids, Cholesterol.*

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Introduction

Breast cancer is the most common cancer in women worldwide and the second leading cause of cancer death among women in America (1). Reports have shown that in 2008, 23% of all new cases of cancer were breast cancer (2). Despite the many advances in early detection and treatment of breast cancer, with higher rates of incidence and mortality of this disease is still considered as one of the major challenges is human society (3). In Iran, as in other developed countries, breast cancer is the most common cancer in women. Recent studies in our country shows that the highest incidence of breast cancer in women between the ages of 49 -40 years old. Breast cancer in women and the incidence of 22 cases per hundred thousand women 84-15 years old, 120 people have been reported (4).

In addition to genetic factors, environmental factors such as diet, obesity, physical activity and alcohol consumption can also be a risk factor to be considered in the development and progression of breast cancer (7-5). Diet, especially eating too much fat and cholesterol, can increase the risk of breast cancer progression (9, 8).

Several studies have done to evaluate changes in serum lipids in patients with breast cancer. Investigations conducted on serum lipids in different regions demonstrated different types of blood lipids had higher levels in women with breast cancer, but not to the same conclusion and a particular type of lipid was effective for each study (10-14).

The results of existing studies indicate that about some serum lipids including total cholesterol, there is no consensus, so Jalilian et al. noted to higher cholesterol levels in patients with breast cancer than the control group (15). In contrast, total cholesterol in some studies in breast cancer patients than the healthy group was significantly lower (16, 17). In addition, Kumar et al. indicated that concentrations were higher (14), but in another study did not observe a significant difference in cholesterol levels between breast cancer patients and healthy individuals (18, 19). Abnormal increase of cholesterol levels in some malignancies is a characteristic (20, 21).

One of the main ways for excretion of cholesterol from the body is to turn it into bile acids (22). In addition to the role of bile acids in solution and absorption of lipids and fat-soluble compounds, it will play an important role in the removal of cholesterol from the body with the solution of cholesterol in bile (22). According to the results of different studies on the cholesterol in breast cancer patients and the importance of bile acid excretion of cholesterol from the body as one of the main ways, this study aimed to measure the concentration of total bile acids and cholesterol in breast cancer patients compared with control group.

Methods

This case-control study was done using easy non-random sampling method on 109 breast cancer patients aged 20-80 confirmed by pathological examination and 109 women referred for routine examination to health centers, in the age group similar to control group. To rule out breast cancer in the control group, the American Cancer Society Guidelines was used (1). For breast cancer screening, all subjects underwent physical examination by the doctor about breast mammography on both sides in two perpendicular directions as well as physical examination, mammography and those who had a positive point, were enrolled.

People with a history of liver-biliary disease, history of familial disorders of lipid metabolism, people with underlying medical conditions such as diabetes or chronic kidney failure, as well as those taking medications affecting lipid metabolism or bile acids such as beta blockers, estrogen, thiazides were excluded from this study. After obtaining informed consent, 7 ml fasting blood serum (14-12 hours) were obtained.

After separating the serum from blood samples by centrifugation (1500 g for 10 min), sera to reach the desired number at 80 ° C were kept. The concentration of serum total bile acid was measured by enzymatic method (Diazyme Kit, Germany) and based on conversion of bile acids to 3-keto steroids using enzyme 3-alpha-hydroxy steroid dehydrogenase by a spectrophotometer.

Measurement of serum cholesterol was done using enzymatic kits (Pars Azmoon). Anthropometric indexes such as weight and height were measured using a digital scale and stadiometer Seca wall (with precision kg 0.1 and cm 0.1) with light clothing and without shoes. Body mass index (BMI) was calculated also by dividing weight (kg) by height squared $^{(m2).}$ Data were analyzed using statistical tests, the Mann-Whitney test and T-test and $p<0.05$ was considered significant

Results

In this study, 109 patients with breast cancer with an average age of 49.2±0.9 years and 109 healthy people with an average age of 46.1±1.2 years were enrolled ($p<0.05$, table 1). The mean weight, height and BMI in patients with breast cancer in comparison with control group were not statistically significant ($p>0.05$, table 1). The stage of disease related to patients were uncertain 10.1 %, 0.9 % in stage 0, 0.9% in stage I, 49.5% in stage II, 35.8% in stage III and 2.8% in stage IV. The mean serum total cholesterol concentrations in the patient group and controls were 316.98±15.35 mg/dl 212.08±5.79 mg/dl, respectively (Fig 1; $p<0.001$).

The average concentration of total bile acids in the patient group and control group was 11.67±0.92 and 13.36±0.81 µmol/l per liter, respectively, showed significant differences (Fig 1; $p<0.05$). No significant differences between the mean of bile acids and cholesterol levels in early and advanced stage of breast cancer were observed in patients ($p>0.05$) (table 2).

Table 1. The demographic and anthropometric data of patient and control groups.

Group Value	Control (n=109)	Patient (n=109)	P-value
Age	46.1±1.2	49.2±0.9	0.044
Weight(kg)	74.8±1.6	75.5±1.6	0.743
Height(m)	1.5±0.01	1.6±0.01	0.231
BMI(kg/m^2)	32.6±1.3	30.3±0.53	0.1

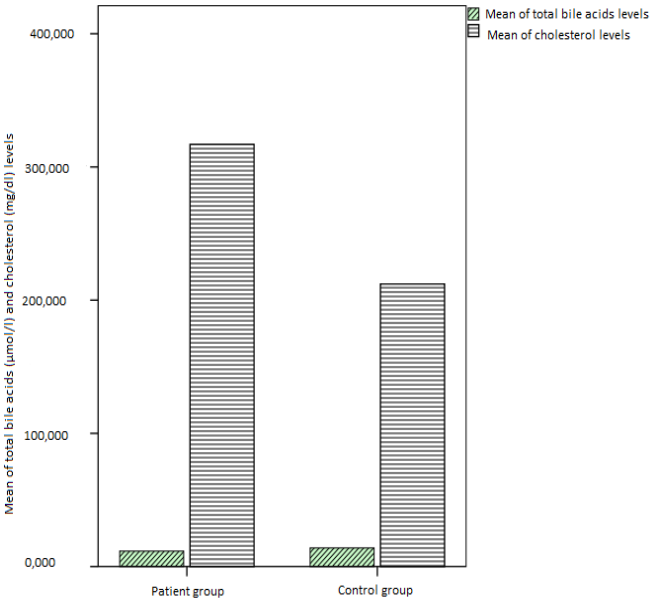

Figure 1. Average concentrations of total cholesterol and bile acids in the case and control groups

Table 2. Average concentrations of total bile acids and cholesterol by age and stage in cases

Variable	Bile Acids (Mean±SD)	P-value	Total Cholesterol (Mean±SD)	P-value
stage				
Early (n=56)	13.6±1.5	0.054	306.4±17.4	0.726
Advanced (n=42)	9.4±1		3.7±25.5	
Age				
<50 (n=55)	12.2±1.4	0.849	305.4±20.4	0.227
50-60 (n=39)	11±1.2		307±22.7	
≥60 (n=15)	11.5±2.8		381.2±55.4	

Discussion

In the present study, the mean serum total cholesterol in patients with breast cancer was significantly higher than the control group. In line with the results, Jalilian et al. showed that cholesterol levels in patients with breast cancer were higher than the control group (15). In another study, researchers showed that serum cholesterol concentrations in patients with breast cancer were higher than the controls (23, 14).

In contrast Agurs-Collins et al. and Martin and colleagues did not report a significant difference in mean serum cholesterol concentration between the case and control groups (24, 11). Franky Dhaval and co-workers and Llanos et al. demonstrated that the concentration of total cholesterol in patients with breast cancer was significantly lower than the control group (17, 16).

In another study, researchers showed an increase in serum total cholesterol in patients with breast cancer before menopause (10). Perhaps one of the reasons for the differences in the results of the studies is genetic differences that can be seen in different geographical areas. Some studies have reported that inhibition of cholesterol in breast cancer cell lines is associated with reduced cell proliferation (25). Thus, in a recent study reported that cholesterol can be considered as a risk factor for breast cancer (25, 9). Also in this study, the mean serum concentration of bile acids in patients with breast cancer was significantly lower than the control group. In contrast, Costarelli et al. in their study did not report no differences in mean serum concentration of bile acids in breast cancer patients and control group (26). Murray et al. in their investigations showed that the total fecal concentration of bile acids in breast

cancer patients is less than controls (27). Bile acids are the end products of cholesterol metabolism in the liver which are necessary to absorb fats and fat-soluble vitamins and maintain a balance between cholesterol synthesis and secretion (22). The conversion of cholesterol to bile acids is very important in controlling the total amount of cholesterol (22). Micellar solubility of cholesterol in the bile through the bile acids, cholesterol, enabling the liver cells and eventually to remove the intestinal tract moving through the pass (22). Due to lower average concentration of total bile acids in patients with breast cancer and higher cholesterol levels in patients compared to controls, it can be suggested that in these patients, lower levels of cholesterol in the body is converted to bile acids. On the other hand it can be hypothesized that a greater amount of cholesterol in the body may be converted to other steroidal compounds such as estrogens, although there is no study in this field.

In total, more studies about the relationship between the concentration of total bile acids and serum total cholesterol and breast cancer as well as other derivatives of cholesterol and is recommended in patients at risk.

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References

1.Richie RC, Swanson JO. Breast cancer: a review of the literature. J Insur Med. 2002;35(2):85-101.

2.Amadou A, Hainaut P, Romieu I. Role of obesity in the risk of breast cancer: lessons from anthropometry. J Oncol. 2013. ID:906495.1-19

3.Howell A, Sims AH, Ong KR, Harvie MN, Evans DGR, Clarke RB. Mechanisms of disease: prediction and prevention of breast cancer—cellular and molecular interactions. Nat Clin Pract Oncol. 2005;2(12):635-46.

4.Mousavi SM, Montazeri A, Mohagheghi MA, Jarrahi AM, Harirchi I, Najafi M, et al. Breast cancer in Iran: an epidemiological review. Breast J. 2007;13(4):383-91.

5.Dal Maso L, Zucchetto A, Talamini R, Serraino D, Stocco CF, Vercelli M, et al. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. Int J Cancer. 2008;123(9):2188-94.

6.Babaei Z, Moslemi D, Parsian H, Khafri S, Pouramir M, A M. Relationship of obesity with serum concentrations of leptin, CRP and IL-6 in breast cancer survivors. J Egypt Natl Canc Inst. 2015;27(4):223-9.

7.Halimi M, Parsian H, Asghari SM, Sariri R, Moslemi D, Yeganeh F, et al. Clinical translation of human microRNA 21 as a potential biomarker for exposure to ionizing radiation. Transl Res. 2014;163(6):578-84.

8.Boyd N, Stone J, Vogt K, Connelly B, Martin L, Minkin S. Dietary fat and breast cancer risk revisited: a meta-analysis of the published literature. Br J Cancer. 2003;89(9):1672-85.

9.Nelson ER, Chang CY, DP M. Cholesterol and breast cancer pathophysiology. Trends Endocrinol Metab. 2014;25(12):649-55.

10.Abu-Bedair FA, El-Gamal BA, Ibrahim NA, El-Aaser AA. Serum lipids and tissue DNA content in egyptian female breast cancer patients. Jpn J Clin Oncol. 2003;33(6):278-82.

11.Agurs-Collins T, Kim KS, Dunston GM, Adams-Campbell LL. Plasma lipid alterations in African-American women with breast cancer. J Cancer Res Clin Oncol. 1998;124(3-4):186-90.

12.Furberg AS, Jasienska G, Bjurstam N, Torjesen PA, Emaus A, Lipson SF, et al. Metabolic and hormonal profiles: HDL cholesterol as a plausible biomarker of breast cancer risk. the norwegian EBBA study. Cancer Epidemiol Biomarkers Prev. 2005;14(1):33-40.

13.Kokoglu E, Karaarslan I, Karaarslan HM, Baloglu H. Alterations of serum lipids and lipoproteins in breast cancer. Cancer Lett. 1994;82(2):175-8.

14.Kumar K, Sachdanandam P, Arivazhagan R. Studies on the changes in plasma lipids and lipoproteins in patients with benign and malignant breast cancer. Biochem Int. 1991;23(3):581-9.

15.Jalilian M Heydari AR. Comparision of the plasma lipid levels in breast cancer patients with control group. Zahedan J Res Med Sci. 2007;9:45-51.

16.Franky Dhaval SSN, Shukla Pankaj Manubhai, Shah, Patel HRPS, Patel. Significance of alterations in plasma lipid profile levels in breast cancer. Integr Cancer Ther. 2008;7(1):33-41.

17.Llanos AA1, Makambi KH, Tucker CA, Wallington SF, Shields PG, Adams-Campbell LL. Cholesterol, lipoproteins, and breast cancer risk in African American women. Ethn Dis. 2012;22(3):281-7.

18.Goodwin PJ, Boyd NF, Hanna W, Hartwick W, Murray D, Qizilbash A, et al. Elevated levels of plasma triglycerides are associated with histologically defined premenopausal breast cancer risk. Nutr Cancer. 1997;27(3):284-92.

19.Fiorenza AM BA, Sommariva D. Serum lipoprotein profile in patients with cancer. A comparison with non-cancer subjects. Int J Clin Lab Res. 2000;30:141-5.

20.Iso H, Ikeda A, Inoue M, Sato S, Tsugane S. Serum cholesterol levels in relation to the incidence of cancer: the JPHC study cohorts. Int J Cancer. 2009;125(11):2679-86.

21.Nelson ER, Wardell SE, Jasper JS, Park S, Suchindran S, Howe MK, et al. 27-Hydroxycholesterol links hypercholesterolemia and breast cancer pathophysiology. Science. 2013;342:1094-8.

22.Monte MJ, Marin JJ, Antelo A, Vazquez-Tato J. Bile acids: chemistry, physiology and pathophysiology. World J Gastroenterol. 2009;15(7):804-16.
23.Ray G, SA H. Role of lipids, lipoproteins and vitamines in women with breast cancer. Clin Biochem. 2001;34(1):71-6.
24.Martin LJ, Melnichouk O, Huszti E, Connelly PW, Greenberg CV, Minkin S, et al. serum lipids, lipoproteins, and risk of breast cancer: a nested case-control study using multiple time points. J Natl Cancer Inst. 2015;107(5).
25.Raza S, Ohm JE, Dhasarathy A, Schommer J, Roche C, Hammer KD, et al. The cholesterol metabolite 27-hydroxycholesterol regulates p53 activity and increases cell proliferetion via MDM2 in breast cancer cells. Mol Cell Biochem. 2015;410(1-2):187-95.
26.Costarelli V, Sanders T. Plasma deoxycholic acid concentration is elevated in postmenopausal women with newly diagnosed breast cancer. Eur J Clin Nutr. 2002;56(9):925-7.
27.Murray WR, Blackwood A, Calman KC, C M. Faecal bile acids and clostridia in patients with breast cancer. Br J Cancer. 1980;42(6):856-60.