Cholesterol Levels in Patients with Chronic Lymphocytic Leukemia

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Abstract: Low cholesterol levels may be accompanied by solid tumors or hematological malignancies such as multiple myeloma. Decreased cholesterol levels have been reported in some experimental studies about chronic lymphocytic leukemia (CLL). It may be associated with tumoral cell metabolism. Herein, we examine blood lipid profiles of patients with newly diagnosed CLL (284 male, 276 female, mean age 64 ± 11 years) as defined by National Cancer Institute criteria. The control group consisted of 71 healthy subjects with mean age 55 ± 9 years (28 male, 43 females). 60% of patients with Binet A, while 25% were Binet C. Decreased levels of total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) were observed in patients with CLL than control group (p < 0,001). There was no statistical significance between CLL and control group for triglycerides (TG) and very low density lipoprotein (VLDL), also between HDL-C, VLDL, TG and grades. Cholesterol may metabolized by abnormal lymphocytes in CLL patients.

Keywords: Blood lipid profiles ■ Cholesterol levels ■ Chronic lymphocytic leukemia

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INTRODUCTION

Chronic lymphocytic leukemia (CLL) is most common type of adulthood leukemias characterized by increased lymphocyte counts and clonal expansion of CD5^{+} B cells in peripheral blood, bone marrow, lymph node, spleen or other organs.[1] Cholesterols play an important role on cancer cells' growth and proliferation. Especially, mevalonic acid is involved in the transition from G1 to S phase.[2] Hypocholesterolemia have been described as laboratory abnormality for pyelonephritis, pneumonia or hyperthyroidism.[3] Also, it may present during the course of malignant disorders such as hematological (acute/chronic leukemia, lymphoma, multiple myeloma, etc.) and solid (gastrointestinal, squamous cell and small cell lung cancer, etc.).[4–7] Cancer cells may lead low density lipoprotein (LDL)/LDL receptor-related protein overexpression. The other factors such as increased uptake of LDL, high density lipoprotein or cholesterol ester have been implicated. Also, suppressing the synthesis of cholesterol was reported in leukemic cells.[8,9] In literature, there were limited clinical studies about hypocholesterolemia and CLL.[10–13] We aimed here to determine correlation between cholesterol levels and its relationship in patients with CLL.

MATERIAL AND METHODS

Patients

Five hundred and sixteen patients who admitted to 9 different hematology centers with the diagnosis of CLL according to the criteria of "National Cancer Institute criteria" were enrolled to this study. Patients with medical history of hypo-hyperthyroidism were excluded from the study. Also, there was no medical history about gastrointestinal absorption disorder, malnutrition and hereditary lipidosis diagnosed by symptoms and physical examination. The control group composed of healthy adults without malnutrition, renal failure, nephrotic syndrome/proteinuria, hypo/hyperthyroidism, chronic diarrhea/malabsorption, familial hypercholesterolemia, and drugs affecting cholesterol or bile acid metabolism. Seventy one (28 male and 43 female with mean age 55 ± 9 years) healthy subjects were included to this retrospective study as control group. The control group was paired for age, sex, and body mass index.

Methods

CLL was diagnosed with the presence of at least 5×10^9 B lymphocytes/L (5000/μL) on peripheral blood and the clonality of the circulating B lymphocytes were confirmed

by flow cytometry. Venous blood samples were taken under the supervision of medical personnel. Whole blood cell count was measured by Coulter Gene-S instrument (Beckman Coulter, California, USA), and the level of total cholesterol (TC), HDL, triglyceride (TG) by Architect C8000 instrument and kits (Abbott, Illinois, USA). Also, LDL-C levels were calculated according to Friedewald Formula ($C_{LDL} = C_{plasma} - C_{HDL} - TG/5$).[14]

Statistical methods

Demographical data about CLL and lipid parameters were recorded. Student's t-test was used for comparison of the normally distributed parameters between the groups in addition to descriptive statistical methods (mean ± standard deviation) during the assessment of the study data. Student's t-test, One-way ANOVA test were used in statistical evaluations. Tukey and Dunnett tests were performed as post-hoc tests. The statistical analysis was performed by using SPSS (Statistical Package for the Social Sciences).[15] The results were evaluated in 95% confidence interval and at a significance level of $p < 0,05$.

RESULTS

Patients

Five hundred and sixteen (284 male and 276 female) patients with mean age with 64 ± 11 years were enrolled to this study. According to Binet classification, 60% of patients were in stage A, while 25% of them were in stage C. Mean laboratory test results were as follows: hemoglobin: 9.9 ± 2.2 g/dL, hematocrit: 30.2 ± 3.7%, platelet counts: $110 \pm 89 \times 10^3$ mm^{-3}, leukocyte counts: $29 \pm 8 \times 10^3$ mm^{-3}, and lymphocyte counts: $21 \pm 7 \times 10^3$ mm^{-3}. There were 71 healthy subjects as control group (43 female and 28 male with mean age 55 ± 9 years). There was no significant difference in gender and age within 2 groups. Serum TSH, AST and ALT were within normal ranges in CLL and control group. Also there were no statistical differences for these parameters between CLL and control group. The characteristic features of the patients with CLL are shown in Table 1.

Lipid parameters

There was significant difference within 2 groups for TC, LDL and HDL levels ($p < 0,001$), and these parameters were significantly lower in CLL group. But, there was no significant difference between 2 groups for the level of VLDL and TG. The lipid parameters are shown in Table 2.

There was no significant difference between lipid parameters and grade. The levels of TC and LDL in the patients with Binet A were higher than Binet B and Binet C

Table 1. The characteristic features of the patients with chronic lymphocytic leukemia.

Sex (M/F)	284/276
Age (years)	
Mean	64 ± 11
Grade (Binet staging system)	
A	255
B	61
C	104

($p < 0,001$). There were no statistical significant differences for HDL, VLDL, and TG between grades. The level of HDL in the patients with Binet C was lower than control groups ($p < 0,001$). The comparison of lipid parameters between Binet staging system in the patients with CLL chronic lymphocytic leukemia is shown in Table 3.

DISCUSSION

We have shown that lower total cholesterol, HDL and LDL levels in newly diagnosed CLL patients when compared with the control group. However, the levels of triglyceride and VLDL were not different in CLL.

In literature, there are limited studies investigating the cholesterol levels in patients with CLL.[10-13] The lipoprotein consists of phospholipids, triglycerides, and esterified-free cholesterol. Cholesterol synthesis and transduction of cell signals are regulated by free cholesterol.[10] Unesterified cholesterols are located on surface, while hydrophobic

Table 2. Lipid parameters between the patients with chronic lymphocytic leukemia and control group.

	Chronic lymphocytic leukemia (n = 560)	Control group (n = 71)	P value
Total cholesterol (mg/dL)	175 ± 42	217 ± 36	<0.001
HDL-cholesterol (mg/dL)	37 ± 11	53 ± 14	<0.001
LDL-cholesterol (mg/dL)	107 ± 31	131 ± 29	<0.001
Triglyceride (mg/dL)	140 ± 71	147 ± 68	>0.05
VLDL-cholesterol (mg/dL)	30 ± 17	31 ± 17	>0.05