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Determination of Lipids Levels among Patients with Chronic Lymphocytic Leukemia in Kurdistan Region of Iraq

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Abstract

Objective: Hypocholesterolemia is a metabolic disorder that can occur in malignancies. Distinct dyslipidemia profiles have been demonstrated in adult and pediatric hematologic malignancies. The aim of this study to assess the lipid profile of patients diagnosed with chronic lymphocytic leukemia. Methods: We assessed lipid profile of Fifty-one patients with chronic lymphocytic leukemia were attended two hematology laboratory facilities of hospital in Erbil and Duhok governorates. Wherever, total cholesterol, triglyceride (TG) values, Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL) were analyzed. For statistical analysis, the student's t-test and the One-way ANOVA test were utilized. In order to do the statistical analysis, SPSS version 26 was used. 95% confidence intervals and a significance threshold of p 0.05 were used to analyze the results. Results: Total cholesterol, LDL and HDL levels were significantly lower in the study group in conjunction with the progression of the disease stages ($p<0.01$). Conclusion: Hypocholesterolemia and low LDL and HDL levels can occur in chronic lymphocytic leukemia. It should be borne in mind that malignancies may be the etiology of unexpected hypocholesterolemia and hypertriglyceridemia. The impact of dyslipidemia on the pathogenesis and prognosis of chronic lymphocytic leukemia requires further study.

Keywords
Chronic Lymphocytic Leukemia (CLL), Dyslipidemia, Hypocholesterolemia, Blood lipid profiles

Background: Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in adults is characterized by number of lymphocytes and clonal proliferation of CD5 B cells in the peripheral blood, bone marrow, lymph nodes, spleen, or other organs (1). CLL is the most common adult leukemia in Western countries. It is more common in men and the age of diagnosis is 72 years old. The incidence rate in Western countries is 10-20 times that Asia countries, suggesting that genetic, environmental or both factors may contribute to the influence Susceptibility to disease (2). Chronic lymphocytic leukemia a collection of clonal neoplastic disorders characterized by the growth of mature B or T lymphocytes (3).

Cholesterol is a key chemical required for cell structure maintenance and is essential for many regular biological activities. It plays an important role in lifestyle-related disorders such as obesity, diabetes,

cardiovascular disease, and cancer (4). The development and reproduction of cancer cells are significantly influenced by cholesterols. Mevalonic acid, in particular, implicated in the change from G1 to S phase (5). According to laboratory findings, pyelonephritis, pneumonia, or hyperthyroidism have been linked to hypocholesterolemia (6).

As one of two indicators of cancer, it can manifest symptoms such as hematological diseases such as leukemia, lymphoma and multiple myeloma; and solid diseases such as lung cancer, gastric cancer or small cell lung cancer. Some other indicators can include the overexpression of LDL/LDL receptor-associated proteins in cancer cells, higher intake of LDL or cholesteryl esters and the presence of more than average amounts of both LDL and HDL. Leukemia cells produce less cholesterol as a result of reduced inhibition. Additionally, it has been noted that this phenomenon has been (7-10).

So, this study aimed to investigate the relationship between blood lipid levels of CLL patients.

Material/Subjects/Patients and methods

Material and Methods

Patients

This study, included 51 patients, diagnosed with CLL by the National Comprehensive Cancer Network. They were admitted to two separate hematological facilities in Erbil and Duhok governorates. No patients symptoms related to hypothyroidism, malnutrition or gastrointestinal absorption issues. The research excluded patients with a medical history of inherited lipidosis, gastrointestinal absorption issues or fat malabsorption.

Methods

CLL was diagnosed when 5,000/L or more blood cells were found in a person's peripheral blood stream by flowcytometer and the Beckman automated Coulter DxH 520. Compact biochemical analyzer was used to measure whole determine cholesterol, triglyceride and HDL levels. Finally, the Friedewald algorithm was used to calculate the LDL-C level in plasma (CLDL = Cplasma - CHDL - TG/5) (11).

Statistical Methods

While analysing research data, the Student's t-test was utilized to evaluate parameters were regularly distributed between groups, as well as descriptive statistical approaches description (mean ± standard deviation) for statistical analysis, the student's t-test and the One-way ANOVA test were utilized. In order to do the statistical analysis, SPSS version 26 was used. 95% confidence intervals and a significance threshold of p 0.05 were used to analyze the results.

Results

Patients

Fifty-one individuals, aged 61 to 66 years, were included in this study. According to Binet's classification system, 53% were in Stage A, 27% were in Stage B and 19% were in Stage C. The average age of participants was 61 years with 35 men and 16 women. CLL patients typically have specific features that set them apart from other patients. These can be found in Table 1. Table 1 includes the characteristics of CLL patients and their levels of Serum TSH, AST and ALT.

Table 1: Demographic characteristics of patients with CLL.

Sex (M/F)	(35/16)
Age (years)	
Mean± SD	61± 8
Stage (Binet staging system)/n	
Stage A	27
Stage B	14
Stage C	10
M=male, F=female, SD=Standard Division	

Lipid Parameters

The Stage and lipid characteristics differed significantly from one another. Patients with Binet A had greater TC, LDL, and HDL values than those with Binet B and C (p <0,01). For VLDL and TG, there were no statistically significant variations across classes (P>0.05). Table 2 shows compares the lipid characteristics between the Binet staging system for CLL (chronic lymphocytic leukemia) patients.

Table 2. Comparison of blood lipid parameters in Binet staging system in patients with chronic lymphocytic leukemia.

Parameters	Stage A (n=27)	Stage B (n=14)	Stage C (n=10)	P Value
Total cholesterol (mg/dL)	170±27	140±35	138±45	<0.01
LDL-cholesterol (mg/dL)	98±24	77±24	74±28	<0.01
HDL-cholesterol (mg/dL)	41±14	32±10	28±12	<0.01
Triglyceride (mg/dL)	148±32	149±31	145±38	>0.05
vLDL-cholesterol (mg/dL)	30±8	29±6	29±10	>0.05

Discussion

The current study shown that the level of total cholesterol, HDL-C, and LDL-C significantly lowered coinciding with the progression of the disease. However, the level of triglyceride and vLDL-C were not different in chronic lymphocytic leukemia patients. The majority of adult mammalian cells take up lipids either as free fatty acids or complexed to proteins like low-density lipoproteins from the circulation. These lipids come from dietary sources or are produced by the liver or adipocytes from fatty acids derived from carbohydrates, where they can also be stored in intracellular organelles known as lipid droplets (12). Triglycerides, phospholipids, and esterified-free cholesterol make up the lipoprotein. Free cholesterol controls the production of cholesterol and the transmission of cell signals. Non-esterified cholesterols are found on the lipoprotein's surface, whereas its interior is composed of hydrophobic triglycerides and cholesterol esters. Phospholipids and cholesterol are linked to the fluidity of cellular membrane (13). Chylomicrons are created from dietary triglycerides that are absorbed by tiny intestinal epithelial cells. Increase of triglyceride synthesis in the liver leads to the production of VLDL. Chylomicron and VLDL triglycerides are hydrolyzed by lipoprotein lipase (LPL), which changes converting VLDL into LDL (14). Lipids have a variety of biological activities that support growth, energy, redox equilibrium, and the spread of cancer cells to generate distant metastases, among other aspects of tumor biology (12). Lipids are needed in huge quantities to form biological membranes, which is necessary for cancer cells rapid rate of cell proliferation. The development and reproduction of cancer cells are significantly influenced by cholesterols. CLL is associated with decreased cholesterol levels. Additionally, other hematological disorders such as acute/chronic leukemias, lymphomas, multiple myelomas and solid tumors can cause hypocholesterolemia. This causes gastrointestinal, lung cell and skin cancer known as squamous cell and small cell (7,8). A lipid analysis was performed in 18 people 45 to 65 years old diagnosed with CLL by Mulas et al. The results showed that 97% of them had hematological malignancies (13). Additionally, 530 cancer patients were studied by Fiorenza et al. Over 97% of them had solid tumors; the results showed that over 530 cancer patients had hematological malignancies (6) and in 128 newly diagnosed CLL patients (59 female and 69 male with a mean age of 65,7 ± 8) (15) in some experimental studies about CLL, reported that cholesterol levels have been decreased. There is a higher chance of developing hematological malignancies when LDL levels are lower than 70 mg/dL. There have been reports of lower LDL breakdown rates in CLL cells. According to Shoret et al., there was a 2.4% relative reduction in the risk of hematological malignancy for every 1 mg/dL increase in LDL. High-density lipoprotein cholesterol, often referred to as HDL, removes cholesterol from the endothelium of blood vessels in the liver (16). In contrast, low-density lipoprotein cholesterol, also referred as LDL, is removed from the liver by intermediate-density lipoprotein. IDL is then converted to cholesteryl esters of low-density lipoprotein cholesterol which is then converted to LDL. Low HDL levels are common in cancer patients and leukemia patients, who both release excrete very low-density lipoprotein triglycerides through their livers (9,13,17,18). Mulas and colleagues (13) studied with phytohemagglutinin that promoted cell division in ALL and CLL cells, they found that this resulted in an increase in cholesterol levels. Children with acute lymphoblastic leukemia had elevated triglycerides, VLDL

and normal levels for HDL, LDL and chylomicrons in another study. Sakashita's research demonstrated that chylomicron lipolysis is not affected in CLL patients. Lymphocytes could utilize HDL cholesterol esters via the receptors scavenger receptor class B type 1 (SR-BI) or the lymphocyte receptor for lymphoid protein LRP (19). SR-BI may facilitate the movement of cholesterol across cell membranes (20). Mulas et al., (13) studied with phytohemagglutinin that promoted cell division in ALL and CLL cells, they found that this resulted in an increase in cholesterol levels. In a separate study, Sakashita found that CLL patients don't have problems converting lipids into energy (21). Lorenz et al., (15) found that Rai CLL classification stage correlated with their lipid parameters. Both studies determined that children with CLL have elevated triglycerides, VLDL, and normal levels of chylomicrons and HDL. They also found higher levels of LDL, VLDL and triglycerides in young adults with CLL. Dessi et al. found that higher disease progression in a patient's condition led to lower HDL levels (9). This was noted by Sherwin et al., who reported this trend in patients suffering from neoplastic diseases (22). Additionally, stage of disease progression influenced both LDL and HDL levels. In fact, Sherwin et al. suggested that stage affected mortality rates among patients with neoplasic diseases (22). According to the Binet classification, 53% of our study's patients were in stage A, with 19.6% in stage C. The HDL, LDL and triglyceride levels of patients in Stage C were lower than in patients in Stages A and B. Likewise, in a study by Yavasoglu, et al., (23) showed that the triglyceride, LDL, and HDL levels in Stage C patients were lower than both Stage A and Stage B. Onat et al., (24) found that the average serum TC and TG levels were 177.1 mg/dL and 146.6 mg/dL, respectively. Additionally, males had an average TC level of 184.4 mg/dL and females had an average level of 183.8 mg/dL. Onat et al., (24) also found that the average triglyceride level was 146.6 mg/dL and 131.9 mg/dL for males and females, respectively. Our study lacks information regarding the patients' cholesterol levels prior to diagnosis. However, patients with diseases that could affect cholesterol levels were not included in the study. Furthermore, other limitation is that, our study did not include a control group for comparison with patients

Conclusion

Chronic lymphocytic leukemia may be accompanied by dropped cholesterol levels. This can be due to increased LDL clearance or the use of cholesterol by CLL cells. Higher cholesterol levels can affect the severity and stage of the disease. When For measuring the patient's cholesterol, HDL and LDL levels should be considered. Additionally, clinicians should be careful when assessing patients with other diseases such as blood cancers or malignant hematomas. These conditions should be considered when assessing the patient's measurements of total cholesterol evaluated (HDL and LDL levels). These values can also be used as biochemical or prognostic markers for patients with newly diagnosed CLL.

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