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Serum Lipid Profile Alterations in Acute Leukemia Before and After Chemotherapy

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Abstract

Background: Serum lipids abnormalities have been observed in various forms of cancers including acute leukemia. Investigators report decreased total cholesterol and HDL, and elevated triglyceride in leukemic patients. Limited studies have been performed to discover the correlation between abnormal lipids profile and disease activity in leukemic patients in Iran. This study was done to evaluate the levels of serum lipid in Iranian leukemic patients, before and after chemotherapy.

Patients and Methods: Seventy eight recently diagnosed and non-treated patients with acute leukemia were included in our study. Blood specimens were collected without anticoagulant before and after chemotherapy; serum was separated and total cholesterol, serum triglyceride, high density lipoprotein cholesterol and low density lipoprotein cholesterol were assessed by enzymatic kits. Statistical analysis was performed using SPSS16.0.

Results: The mean age of patients was 24.87 years (range 9-52), with newly diagnosed acute lymphocytic leukemia in 48 patients and acute myeloid leukemia in 30 patients. From the participating patients 42(53.8%) were male and 36(46.2%) were female. Data analysis showed that the mean total cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol, in all age groups and in both sexes, were significantly lower before chemotherapy than after; whereas, the mean triglyceride was higher before therapy than after.

Conclusion: Based on our findings, it seems that lipid profile assessment can be employed as a beneficial prognostic factor in acute leukemia. Besides, it can be a simple, fast and economical method to following up the patients' response to chemotherapy.

Key words: Acute Leukemia, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglyceride.

Introduction

The correlation between levels of serum lipids and cardiovascular diseases had been studied comprehensively and the role of abnormal blood lipid levels had been verified in such diseases [1-3]. Moreover in recent decades, the researchers' attention has been attracted towards studying the role of lipids in different types of malignancies. Decreased blood lipid levels have been observed in various forms of cancer including pancreatic, lung, ovarian and colon cancer; and different hypothesis have been made to explain the pathogenetic mechanisms of these alterations [4,5].

Acute leukemia is a malignant disorder which is created due to clonal expansion of lymphoid and myeloid progenitors. Many surveys have been performed considering the serum lipids abnormalities in acute leukemia and most of them have demonstrated decreased total cholesterol and elevated triglyceride in leukemic patients; nevertheless, changes of different cholesterol

fractions are divers and contradictious [6-13]. Several studies have reported some changes in lipids metabolism at diagnosis time in leukemia. Although investigators have reported decreased total cholesterol, decreased HDL and elevated triglyceride among leukemic patients; there is a controversy about these changes among different types of leukemia and between children and adults with leukemia [6].Limited studies have been performed in order to discover the correlation between abnormal lipids profile and disease activity in leukemic patients [14-16].Some research findings have demonstrated that lipid profile would get back to normal levels after treatment and in complete remission phase which corroborates the correlation between abnormal lipid profile and disease activity. So the lipid profile of leukemic patients can be considered as a possible prognostic or diagnostic factor and might be used as a simple test for following up the patients response to chemotherapy [14-16].

Due to inadequate studies about this subject in Iran [17, 18], this study was carried out to evaluate the level of serum lipids among Iranian patients' who suffer from acute myeloid and lymphoid leukemia; in the time of diagnosis as well as after treatment and complete remission.

Patients and methods

Seventy eight patients with newly diagnosed acute leukemia who were admitted to different hospitals of the Tehran University of Medical Sciences were included to our study. The types of leukemia were determined by oncologists using bone marrow aspiration and other particular tests. This study was approved by the university's ethics committee and before initiating the study, written consent was obtained from each patient. Blood samples were obtained before and after chemotherapy, after an overnight fast. All cases were recently diagnosed and non-treated acute leukemic patients. Blood specimens were collected after conclusive diagnosis and segregated serum was kept in freezer for lipid testing. After chemotherapy, patients were followed up in professional clinical centers; and the other blood specimens were collected after complete remission based on clinical and paraclinical criterion. Among these patients children received chemotherapy with vincristine, adriamycin and asparaginase; and cyclophosphamide, daunorubicin, vincristine and cytosar were prescribed for adult patients. Blood specimens were collected without anticoagulant and serum was separated from RBCs by centrifugation. Triglyceride and total cholesterol were determined using laboratory kits purchased from ZistShimi Company, Tehran Iran. Direct analysis of high density lipoprotein cholesterol (HDLC) was done using ELITECH kits (France). LDL cholesterol direct SL kits from ELITECH Company (France) were used for direct analysis of low density lipoprotein cholesterol. All measurements were done by auto-analyser automatically.

Statistical analysis was performed using SPSS

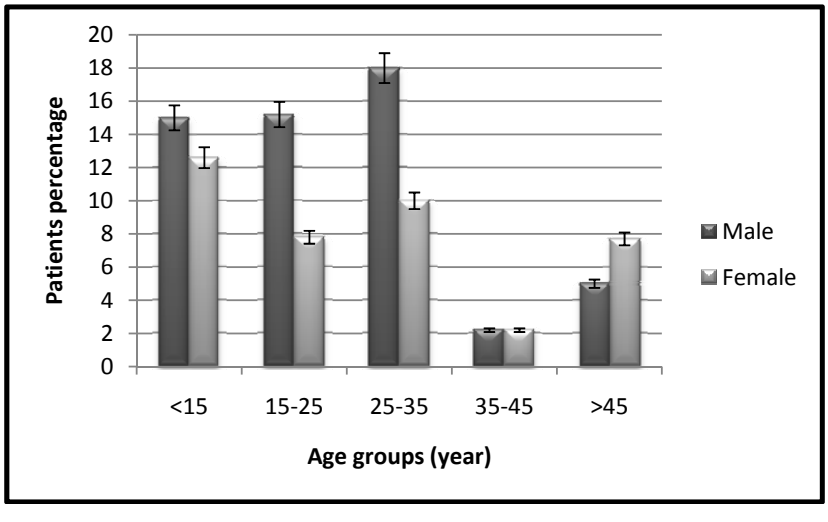

Figure 1: Age and sex distribution of patients with acute leukemia.

version 16.0. Paired T test and Wilcoxon signed-rank tests were used to compare the mean lipid levels at diagnosis and after chemotherapy.

Results

A total of 78 patients, mean age 24.87 years (range 9-52), including 48 newly diagnosed acute lymphoblastic leukemia and 30 acute myeloid leukemia patients were included in our study. From the participating patients 42(53.8%) were male and 36(46.2%) were female. The age and sex distribution of studied patients are presented in figure 1.

The results indicate that the mean serum total cholesterol concentrations among un-treated patients were 112.54, 120.44, 165.40, 107.50 and 122.80mg/dl for the <15, 15-25, 25-35, 35-45, and >45 years age groups respectively. After treatment, the total cholesterol concentrations upraised to 150.80, 155.22, 206.10, 136.50, 172.20mg/dl for these age groups. Comparison of the mean total cholesterol in different age groups, using paired T tests, showed a significant difference (P=0.001) between before and after treatment concentrations (Figure 2).

The mean serum triglyceride concentrations among un-treated patients were 197.08, 197.11, 224.90, 101.00 and 159.00 mg/dl for the <15,

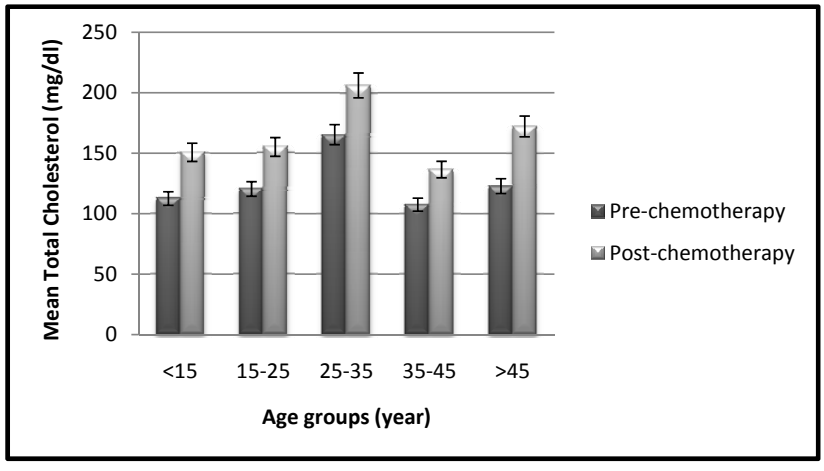

Figure 2: Comparison of the mean total cholesterol levels in different age groups of patients with acute leukemia before and after chemotherapy.

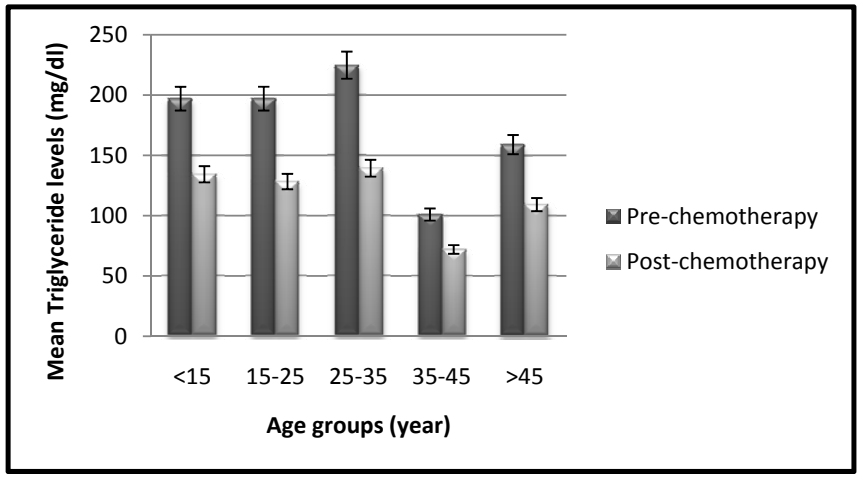

Figure 3: Comparison of the mean triglyceride levels in different age groups of patients with acute leukemia before and after chemotherapy.

15-25, 25-35, 35-45, and >45 years age groups respectively; which decreased to 134.80, 128.33, 139.40, 72.00 and 109.20mg/dl, in treated patients. Comparison of the mean triglyceride in different age groups, using paired T tests, showed significant difference (P=0.003) between before and after treatment concentrations (Figure 3).

The mean serum low density lipoprotein cholesterol among un-treated patients in different age groups was 70.8, 78.00, 107.80, 71.50 and 79.40 mg/dl respectively. After therapy LDLC levels elevated to 105.00, 92.56, 113.40, 84.50, 119.60mg/dl for these age groups. Comparison of the mean LDLC in different age groups, using paired T tests, indicated significant difference (P=0.032) between before and after treatment concentrations (Figure 4).

The mean serum high density lipoprotein cholesterol (HDLC) before treatment was 24.08, 24.10, 25.60, 26.50 and 27.00mg/dl for the <15, 15-25, 25-35, 35-45, and >45 years age groups and after treatment these levels increased to 37.38, 36.00, 40.50, 37.50, 33.60mg/dl respectively. Comparison of the mean HDLC in different age groups, using paired T tests, displayed significant difference (P=0.001) between before and after treatment concentrations (Figure 5).

Data analysis illustrated that the mean total cholesterol, LDLC and HDLC, in all age groups and in both sexes, were significantly lower before therapy than after; whereas, the mean triglyceride, in all age groups and in both sexes, were significantly higher before therapy than after therapy. Table 1 shows comparison of the mean serum lipids of all patients before and after chemotherapy. Statistical analysis using paired T test indicated a significant difference in mean cholesterol, triglyceride, LDLC and HDLC between un-treated and treated groups of patients. Aditionally, Wilcoxon signed-rank test confirmed the significant difference among these parameters before and after chemotherapy (P=0.001).

Discussion

Attempts have been made to evaluate the correlation between serum lipids in leukemic patients and the disease activity and response to chemotherapy [14]. Due to the high rate of expansion and metabolism in cancer cells, cholesterol and other intracellular lipids decrease in these cells. This may lead to over-expression of LDL receptors which causes the serum LDLC to decline. For instance, in malignant cells of AML, LDL uptake increases up to 100 folds [19].

Many researchers have performed studies about the serum lipids abnormalities in acute leukemia which have demonstrated a significant difference in lipid profile compared to normal individuals. First in 1982, Spigel et al., studied the serum lipids changes in leukemia and lymphoma. The data they presented, demonstrated decreased levels of HDLC as well as increased levels of triglyceride and

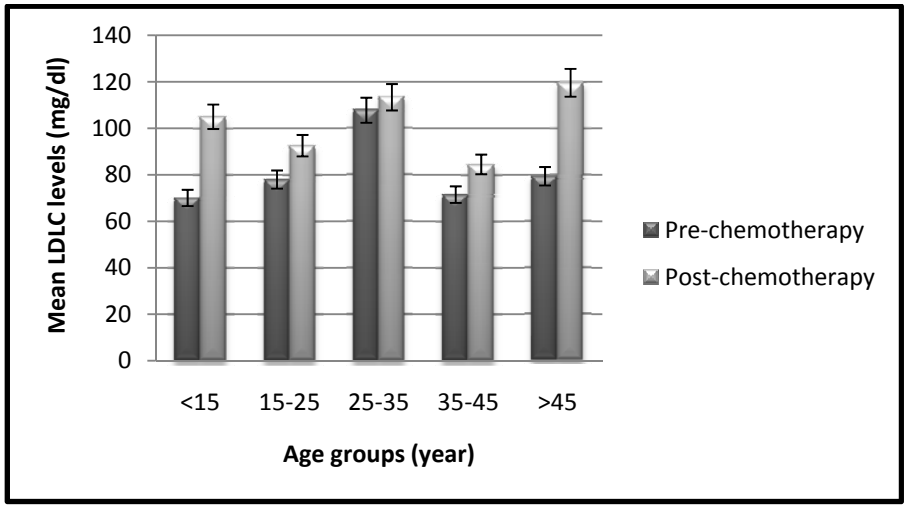

Figure 4: Comparison of the mean LDLC levels in different age groups of patients with acute leukemia before and after chemotherapy.

CLDL-V in relapse phase which gets back to normal levels after remission [10,19]. Favrot et al.[12] and Budd et al.[20] reported hypertriglyceridemia and a decline in total cholesterol, HDLC and LDLC among leukemic patients. Similar results have been observed by Naik et al. [13] (in 55 leukemic patients) and Tao et al.[21] (in 86 ALL patients). Another study by Vesal et al. on children with ALL, showed elevated triglyceride levels and decreased cholesterol and LDLC concentrations in comparison with the control group [17]. In this regard, other researchers have evaluated the lipids profile pre- and post-chemotherapy. Their results indicate that lipids profile is altered in relation to leukemia's activity. In 1996, three different groups indicated that the total cholesterol, HDLC and LDLC are increased after therapy, but triglyceride and VLDL which were high before chemotherapy, would become normal after remission [22-24]. Juliusson et al. reported hypercholesterolemia in hairy cell leukemia patients after treatment [9]. Halton et al. studied lipid profile in children with ALL and realized that triglyceride levels are elevated and HDLC levels are reduced, but there was no significant increase in triglyceride levels after remission [6]. Musolino et al. evaluated the lipid profile in ALL patients and found that the total cholesterol and LDLC levels are lower than normal before chemotherapy; and although they would increase after remission, it will still be lower than normal levels [11].

Moschovi et al. indicated that there is a significant difference in triglyceride, LDLC and HDLC levels between un-treated and treated patients; as LDLC and HDLC levels were low before chemotherapy and increased after remission, but triglyceride was the vice versa [10]. Veena et al. evaluating chronic myeloid leukemia (CML) patients realized that total cholesterol, LDLC and HDLC levels were low before chemotherapy and increased after remission but no significant decline was observed in triglyceride levels after remission [14].

Gokhale et al. compared the lipids profile of children with ALL with a control group. They reported that regardless of the type of treatment, there was no difference between total cholesterol in treated and control groups [15]. Kuliszkiewicz et al. studied 238 cancer patients; 84 of them were ALL patients. They reported that there was a significant difference in lipid levels, especially in HDLC, during the disease and after the remission; and the triglyceride levels is high before treatment [7]. Previous studies have shown that leukemic blood and bone marrow cells from ALL patients can uptake HDLC with a higher rate than normal cells. Total cholesterol, HDLC and LDLC in leukemic patients is lower than normal individuals; but, TG and VLDL show no significant differences [25,26]. Some studies suggest that lipid abnormalities might be due to using some chemotherapy drugs like asparginase [18,27]. Hasan et al. showed that asparginase would cause hypertriglyceridemia; in their study, plasma LDL was significantly increased during therapy with

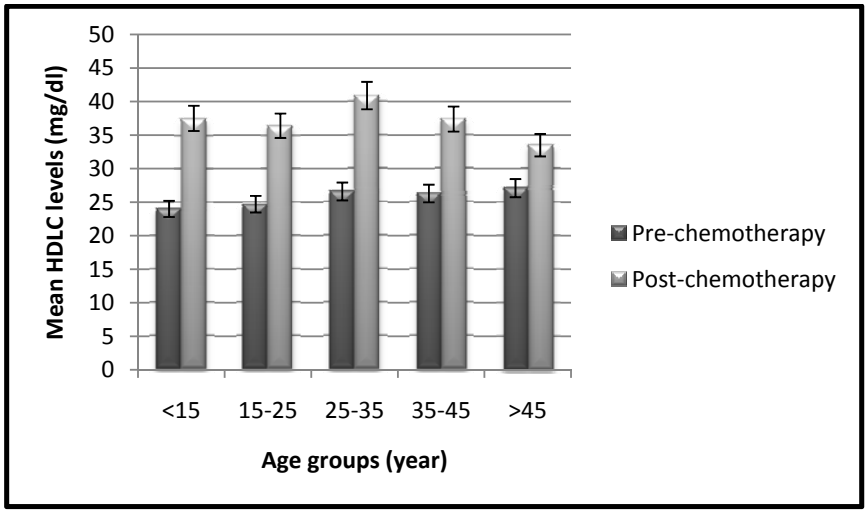

Figure 5: Comparison of the mean HDLC level in different age groups of patients with acute leukemia before and after chemotherapy.

asparginase [28]. Another study performed by Halton et al. indicated extremely elevated TG levels during combination therapy with L-asparaginase and corticosteroid [28].

Cholesterol decline and triglyceride increase are common findings in all these researches. However, there are contradicting findings considering the LDLC and HDLC levels which is probably due to using different calculation methods instead of direct analysis [6,8,14]. Our results were in agreement with most studies in this area [21,23]. In the present study, triglyceride levels decreased after chemotherapy; similar results were observed by Tao et al. and Naik et al [13, 21]. Total cholesterol was lower than normal range before chemotherapy, in all age groups and rose significantly after chemotherapy and in remission phase. This was in agreement with findings of Tao et al. and Moschovi et al. and in contrast with findings of Gokhale et al [10,13,15].

In the present study, HDLC and LDLC levels before chemotherapy were lower than their levels after therapy and both parameters elevated significantly after remission. Our findings about HDLC were in agreement with findings of Kuliszkiewicz et al [7]. It is remarkable that in most studies LDLC levels were obtained by calculation method, but in our study they were obtained by direct analysis. We think due to the abnormal lipid profile in leukemic patients and the usage of triglyceride concentration in LDLC calculation formula, our results are more reliable than the others.

Conclusion

Based on our findings, it seems that lipid profile assessment can be employed as beneficial prognostic factor in acute leukemia. Besides, it can be a simple, fast and economical method to following up the patients' response to chemotherapy.

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Table 1: Comparison of serum lipids concentrations (mean±SD) pre- and post- chemotherapy.

Serum lipids*	Pre-chemotherapy	Post-chemotherapy	P Value
cholesterol	128.97 ± 8.53	168.01 ± 11.66	0.000
triglyceride	194.41± 18.28	127.85 ± 8.59	0.000
HDLC	25.31 ± 1.22	37.38 ± 1.78	0.000
HDLC	82.85 ± 6.76	105.10 ± 6.41	0.032

*All values are expressed in milligrams per deciliter.

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