

Lipid Profile, Serum Ferritin and Dyslipidemia in Survivors of Acute Lymphoblastic Leukemia

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Abstract

Background:The most common type of cancer in children is acute lymphoblastic leukemia ALL. Hereditary hemochromatosis (HH), a hereditary iron metabolic condition associated with tissue damage, is the major cause of elevating iron tissue concentration. The study aimed to Lipid profile, serum ferritin and dyslipidemia in Survivors of Acute Lymphoblastic Leukemia. **Methods:**This study was conducted at pediatric oncology out patient clinic at **Children Hospital Zagazig university & The Scientific Research Centre of Faculty of Medicine Zagazig university** during the period from the 1st of July 2017 to the 15th of April 2018 on 50 of ALL survivors including 26 male & 24 female and in addition 50 age and sex matched children were included as control group. **The following investigations were done: CBC, Serum ferritin and Fasting lipid profile. Results:**Serum ferritin was significantly higher in ALL survivors than the control. In the current study, lipid profile including serum cholesterol, serum triglycerides, serum LDL showing higher significance difference in ALL survivors than control group, while serum HDL is significantly lower in ALL survivors than control group. Concerning dyslipidemia among ALL survivors group, HDL was < 40 mg/dl among 10% and TG was above 150 mg/dl in 18% of the studied patients, all of them their cholesterol level is less than 200 mg/dl, and LDL was less than 130 mg/dl. **Conclusion:** Serum ferritin was significantly higher in ALL survivors than the control. lipid profile including serum cholesterol, serum triglycerides, serum LDL showing higher significance difference in ALL survivors than control group, while serum HDL is significantly lower in ALL survivors than control group. Higher dyslipidemia among ALL survivors group.

Key words: Lipid profile, serum ferritin- dyslipidemia- Acute Lymphoblastic Leukemia.

Introduction:

The most common type of cancer in children is acute lymphoblastic leukemia ALL⁽¹⁾.

Several studies recorded that cardiotoxicity developed in All survivors previously treated with doxorubicin chemotherapy during their disease⁽²⁾.

Several risk factors included in the production of cardiotoxicity of doxorubicin such as girls ' down syndrome, younger age, higher dose and cumulative dose⁽³⁾.

In other words, doxorubicin cardiotoxicity also induces doxorubicin-iron complexes, which transform into a semiquinone-free radical that interacts with oxygen and contributes to lipid peroxidation and DNA damage.

In other words, elevated concentration of iron tissue increases the risk of developing doxorubicin cardiotoxicity proves to be useful if iron chelating agent as dexrazoxane precedes the treatment of doxorubicin chemotherapy, as this decreases the concentration of iron tissue and subsequently free radical formation⁽⁴⁾.

Hereditary hemochromatosis (HH), a hereditary iron metabolic condition associated with tissue damage, is the major cause of elevating iron tissue concentration. ⁽⁵⁾.

The study aimed to Lipid profile, serum ferritin and dyslipidemia in Survivors of Acute Lymphoblastic Leukemia

Patients and Methods

➤ **Technical Design**

- ◆ **Site:** This study was conducted at pediatric oncology out patient clinic at **Children Hospital Zagazig university & The Scientific Research Centre of Faculty of Medicine Zagazig university** during the period from the 1st of July 2017 to the 15th of April 2018 on 50 of ALL survivors including 26 male & 24 female and in addition 50 age and sex matched children were included as control group.
- ◆ Study was approved by IRB.
- ◆ Consent was obtained from parents of both ALL survivors and control group.
- ◆ **Type of study:** Observetional Cross section case control study.
- ◆ **Population:** Fifty of acute lymphoblastic leukamia survivors previously treated with doxorubicion and in addition 50 age and sex matched children were included as control group.

Inclusion criteria:

- Survivors of ALL children treated with chemotherapy protocol CCG including doxorubicion.
- Finished chemotherapy for more than one year.

Exclusion criteria:

- ALL patient still on chemotherapy.
- Patient with other cancer.
- ALL patients with chronic liver disease.
- ALL patients with chronic renal disease.
- ALL survivors with congenital heart disease.
- ALL patients with Diabetes millitus .

Sample size:

Assuming that the total number of acute lymphoblastic leukemia survivors attending pediatric out patient clinic for follow up is 50 cases per 6 monthes (according to 2017 attendance rate), all cases were included and 50 apparently healthy children as control.

➤ **Operational Design**

(a) All survivors enrolled in this study were subjected to:

- Detailed history.
Thorough clinical and physical examination.

a) Anthropometric measurement including estimation of body mass index (BMI)

- ◆ **Laboratory investigation:** All were investigated at Sientific Medical Search Center of Zagazig University Hospital
- ◆ **Blood sampling:** 3ml venous blood sample were collected for each child on sterile polyethelene plastic tube without anticoagulant and serum was separated after clot formation and stored at -20c till assay of Fasting lipid profile and Serum iron ferrittin.

- **CBC**
- **Serum ferritin**
- **Fasting lipid profile**

Analyte	Reference Range
Total cholesterol	140–200 mg/dL (3.6–5.2 mmol/L)
HDL-C	40–75 mg/dL (1.0–2.0 mmol/L)
LDL-C	50–130 mg/dL (1.3–3.4 mmol/L)
Triglycerides	60–150 mg/dL (0.7–1.7 mmol/L)

(6)

Statistical Analysis

- The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 16.0 (SPSSInc., 2007). For the statistical calculations data coding was done.
- Qualitative data were represented as frequencies and percentages, Chi- Square test (χ^2) and fisher exact test were carried out for testing the association between the qualitative data frequencies.
- Quantitative data were represented as mean, standard deviation (SD) and median, student's t-test was used to detect difference between groups which were normally distributed and MannWhitney test was used to detect the difference between groups which were not normally distributed.
- The test results were considered significant when $p\text{-value} \leq 0.05$, highly significant when $p\text{-value} \leq 0.01$ and non significant when $p\text{-value} > 0.05$. All p values are two-tailed.

Results:

This table shows that the mean age of the studied ALL survivors patients is 12.156 ± 2.92 years old, with a range from 7 to 10 years old, and age of healthy control is (12.1 ± 2.8 yrs. old), there is no statistically significant difference between ALL survivors and control group regarding age and sex(**Table 1**).

This table shows that the mean of BMI among the studied ALL survivors is 21.9 ± 1.49 (kg/m^2), with a range from 21 to 27and BMI of control is 18 ± 3.36 (kg/m^2), with highly statistically significant difference between ALLsurvivors and control group regarding BMI, (**Table 2&figure 1**).

Table (3) showingthatmean WBCs among the studied ALL survivors is $8.34 \pm 2.14 \times 10^3/\text{u/L}$, and it is $8.93 \pm 1.72 \times 10^3/\text{u/L}$ among control group with no statistically

significant difference between ALL and healthy control regarding WBCs and Platelet count but Hemoglobin level and ANC among ALL survivors were statistically significant lower than control group.

This table shows that lipid profile parameters and ferritin level were statistically higher among ALL survivor, than control group. (**Table 4**).

Concerning dyslipidemia among the studied group, HDL was < 40 mg/dl among 10% and TG was above 150 mg/dl in 18% of the studied patients, all of them their cholesterol level is less than 200 mg/dl, and LDL was less than 130 mg/dl(**Table 5**).

Table (1): Demographic data of the studied survivors of ALL children and control group.

Demographic data	ALL (N=50)		Control (N=50)		MWT/ χ^2	P- value
Age (years)						
Mean $\pm$ SD	12.156 $\pm$ 2.92		12.1 $\pm$ 2.8		1223.5	0.854 (NS)
Median (Range)	12 (7-18)		12 (6-17)			
Sex						
	No.	%	No.	%		
Male	26	52.0	30	60.0	0.649	#0.546 (NS)
Female	24	48.0	20	40.0		

MWT: Mann Whitney U test.

χ^2 : Chi-square test.

P < 0.05 is significant.

NS: Not significant.

Table (2): BMI (body mass index) among the studied groups

BMI	ALL (N=50)		control(N=50)		MWT/ χ^2	P- value
	No.	%	No.	%		
BMI (kg/m2)						
Mean $\pm$ SD	21.9 $\pm$ 1.46		18 $\pm$ 3.36		466.00	0.000* (HS)
Median (Range)	21 (21-27)		18 (16-25)			

MWT: Mann Whitney U test.

χ^2 : Chi-square test.

*P < 0.05 is significant.

NS: Not significant.

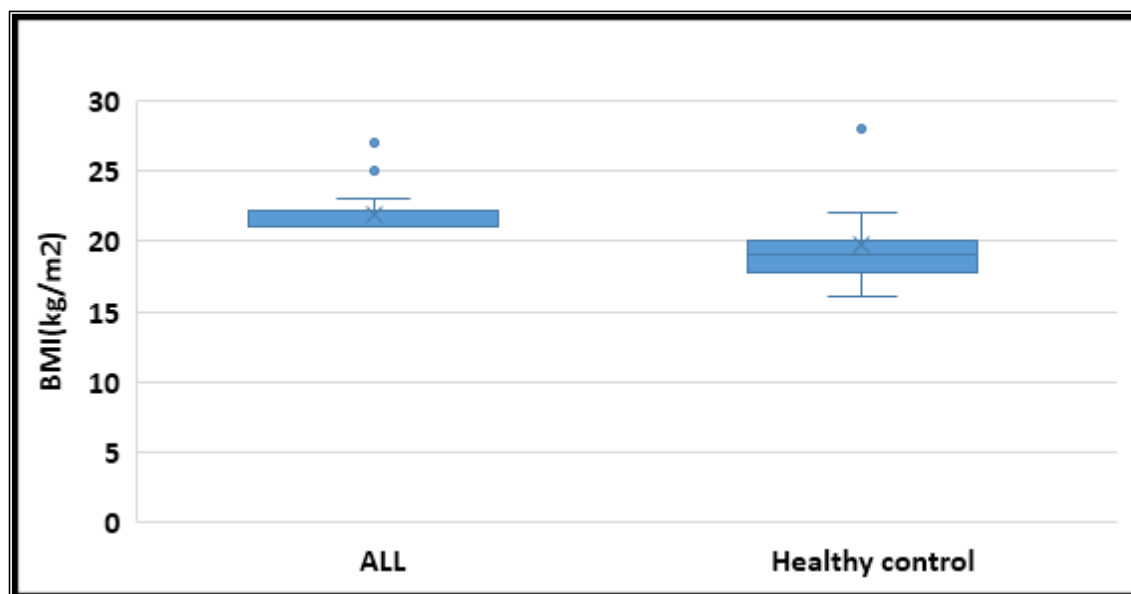


Figure (1): Box plot showing BMI among the studied groups

Table (3): Hematological findings among the studied groups

Hematological findings	ALL (N=42)	control(N=42)	MWT	p-value
Hemoglobin (mg/dl)				
Mean ± SD	11.6±0.71	12.71±0.68	420.000	0.000* (HS)
Median (Range)	12(9.9-12.6)	12.8(11.5-13.6)		
WBCsX10 ³ u/L				
Mean ± SD	8.34±2.14	8.93±1.72	1080.00	0.240 (NS)
Median (Range)	8.88(4.2-11.3)	9.2(5.6-10.8)		
ANCX10 ⁶ u/L				
Mean ± SD	1.98±0.48	2.36±0.33	670.00	0.000* (HS)
Median (Range)	1.9(1.05-2.8)	2.3(1.9-2.8)		
Platelet countX10 ³ u/L				
Mean ± SD	289.94 ±88.4	298.7 ± 68.55	1220.00	0.836 (NS)
Median (Range)	303(145-432)	294.4(199-420)		

Mann Whitney U test.

P < 0.05 is significant.

NS: non-significant.

ANC: absolute neutrophil count

WBCs: white blood cells

Table (4): Lipid profile and serum Ferritin among the studied groups..

Parameters		ALL (N=50)	Healthy control(N=50)	P- value
Lipid profile				
Cholesterol (mg/dl)	Mean $\pm$ SD	144.49 $\pm$ 27.6	79.15 $\pm$ 12.77	0.000* (HS)
	Median (Range)	144.7 (98.3-191)	80.1(55-102)	

LDL (mg/dl)	Mean ± SD	104.19 ± 13.7	65.59±16.08	0.000* (HS)
	Median (Range)	103.1(82.9-129)	62.6(48-103.2)	
HDL (mg/dl)	Mean ± SD	22.8 ± 7.9	46.8±6.7	0.040* (S)
	Median (Range)	22(17-41)	37(37-48)	
TG (Triglycerides) (mg/dl)	Mean ± SD	106.3 ±46.9	70.3±22.3	0.000* (HS)
	Median (Range)	87.3(68-292)	75(38-134)	
Serum Ferritin (ng/dl)				
Serum Ferritin	Mean ± SD	156.65±162.8	46.4±19.43	0.000* (HS)
	Median (Range)	103.45(32-1011)	49(13.7-81)	

*Mann Whitney U test.**P < 0.05 is significant.**AST:aspartate aminotransferase**HS: highly significant.**TSB:total serum bilirubin**ALT:alanine aminotransferase**HDL /LDL:high/low density lipoprotein***Table (5): Dyslipidemia among the studied ALL survivors**

Dyslipidemia	ALL cases(N=50)	
	No.	%
Cholesterol > 200 mg/dl	0	0.0
LDL > 130 mg/dl	0	0.0
HDL < 40 md/dl	5	10.0
TG > 150 mg/dl	9	18.0

Discussion

Serum ferritin was significantly higher in ALL survivors than the control. This is may be related to repeated blood transfusions. A commonly cited pathway involves anthracycline-induced generation of reactive oxygen species (ROS).

There is evidence that anthracyclines catalyze the formation of intracellular oxygen radicals through the nonenzymatic pathway, anthracyclines may directly react with ferric iron (Fe³⁺), leading to free radical and, producing ROS ⁽⁷⁾.

In the current study, lipid profile including serum cholesterol, serum triglycerides, serum LDL showing higher significance difference in ALL survivors than control group, while serum HDL is significantly lower in ALL survivors than control group.

Concerning dyslipidemia among ALL survivors group, HDL was < 40 mg/dl among 10% and TG was above 150 mg/dl in 18% of the studied patients, all of them their cholesterol level is less than 200 mg/dl, and LDL was less than 130 mg/dl.

Morel et al.⁽⁸⁾ results show that, despite their young age, 50% of the ALL survivors displayed dyslipidemia, characterized by increased plasma triglyceride (TG) and LDL-cholesterol, as well as decreased HDL-cholesterol and obesity compared to control groups.

Many studies reported similar results as^(9; 10; 11; 12; 13).

Conclusion:

Serum ferritin was significantly higher in ALL survivors than the control. lipid profile including serum cholesterol, serum triglycerides, serum LDL showing higher significance difference in ALL survivors than control group, while serum HDL is significantly lower in ALL survivors than control group. Higher dyslipidemia among ALL survivors group.

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