Biological markers study of acute and chronic myeloid leukemia

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ABSTRACT

Twenty two acute myelogenous leukemia (AML) patients and 20 chronic myelogenous leukemia (CML) patients, were admitted to Medical City Hospital, in addition to 35 healthy individuals as the control group. Vitamin C and vitamin D, trace and essential elements cobalt, and Nickel magnesium were evaluated in the sera of all above individuals, using high performance liquid chromatography and atomic absorption spectrophotometry for evaluating vitamins and elements. The results revealed a a significant decrease in vitamin C and vitamin D and Mg levels in both patients groups compared to controls and a significant difference in CO and Ni levels in sera of AML and CML was found.

Conclusion: Vitamins, trace and essential elements abnormalities occur in both patient groups compared to Controls.

Key words : Acute, Chronic leukemia, vitamins C, D, cobalt, Nickel, Magnesium

Introduction

Leukemia is a type of cancer of the blood or bone marrow characterized by an abnormal increase of immature white blood cells called “blasts. It is classified into several types. Acute and chronic could be considered as the essential type and includes many types under each term such as lymphocytic, granulocytic and monocytic leukemia((1). Acute leukemia, is one of the two major categories of leukemia, with symptoms including anemia, fatigue, weight loss, easy bruising, thrombocytopenia, and granulocytopenia ,while chronic leukemia is characterized by the excessive build up of relatively mature, but still abnormal, white blood cells (2). The maintenance of optimal health proteins, lipids, macronutrients, micronutrients, vitamins and trace elements.(3) Vitamins are an organic compound required by an organism as a vital nutrient. In limited amounts ,vitamins serve multiple roles and they work together to perform many functions, from reducing infection to aiding metabolism. (4) Vitamin C (Ascorbic Acid) is an important antioxidant found in the biological system. It is the first line antioxidant defense in plasma.(5) Proposed mechanisms of vitamin C activity in the prevention and treatment of cancer include : enhancement of the immune system by increased lymphocyte production, stimulation of collagen formation necessary for “walling off” tumors , inhibition of hyaluronidase, keeping the ground substance around the tumor intact and preventing metastasis, inhibition of oncogenic viruses, correction of an ascorbic deficiency, and is often seen in cancer patients.(6,7,8)

Cholecalciferol is a prohormone that is synthesized in the skin by photochemical conversion of 7-dehydrocholesterol. It is subsequently hydroxylated to 25-hydroxycholecalciferol [25(OH)D3] in the liver and in the kidney finally to the active metabolite, 1,25 didydroxcholecalciferol [1,25(OH)2D3. (9 ,10)

Trace elements (TE) are a group of elements that are present in the human body in very small amounts (milligrams per day), but are nonetheless important to good health .(11)Their action is that (TE) are constituents of, or interact with enzymes, cofactors , phosthetic groups or hormones that regulate the metabolism of much larger amounts of biochemical substrates(12).

Cobalt is an essential element for humana, as a part of vitamin B12 (coblamin) - micro flora of the lumen intestine.1(13,14,15,)

Nickel is one of the ultra trace elements; Nickel ions used in the iron transport system across small intestine related with ferritin, thereby cause anemia;the deficiency of nickel causes alteration of folate and vitamin C .(16)

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Magnesium (Mg) is essential to the basic nucleic acid chemistry of life and thus is essential to all known living organisms. Mg is important for maintaining of DNA. Magnesium is extremely necessary for proper ATP synthesis(17,18,19).

Aim of Study

The aim of the study is to evaluate vitamin C, vitamin D and trace and essential elements of Co, Ni, Mg, levels in the sera of patients with acute and chronic leukemia compared to controls.

- Experimental Part
- Subjects:

Blood samples were collected from the patients with acute myelogenous leukemia (AML) and patients with chronic myeloblastic leukemia (CML) from men, who were admitted to Medical City Hospital. Their age range was 32-52 years. The patients were diagnosed by specialist doctors. Thirty five healthy individuals were matched aged 30-50.

Instrumentation : Vitamin C was measured using high performance liquid chromatography (Shimadzu Japan C18 column) . Vitamin D was separated on FLC (Fast liquid chromatograph column) 3µm particle size stored column, obtaining optimum conditions, temperature, flow rate, eluent composition were used for detection of vitamins . The concentration of each vitamin was estimated through measurement of area under the curve of chromatograms of standard vitamins and for patients and control serum samples.

$C_{standard}$ = Standard concentration of the measured vitamin in ug/ml.

Vitamin concentration in υg/ml = $\frac{A_{sample}}{A_{standard}} \times C_{standard}$

A_{sample} = Area under the curve of sample.

$A_{standard}$ = Area under the curve of standard

Atomic absorption spectrophotometry (model AA46-schma-dzo-japan{AAS) : AAS was used for determination of CO, Ni and Mg. A standard calibration curve is used for measurement of CO, Ni and Mg in the sera of groups under this study AML, CML, and controls.

Statistical analysis

The means and standard deviations, and student t test was used to compare the significance of the difference in the mean values of any two groups.

($P \leq 0.05$) was considered statistically significant (20).

Result and Discussion

Table 1 (opposite page) shows low serum levels of vitamin C (3.06, 3.46 µg|ml) for AML, ACML compared with controls (4.2µg|ml).

It was reported that toxic reactive oxygen species increase during leukemia(21). Ascorbate is a powerful reducing agent capable of rapidly scavenging a number of reactive oxygen species, so our results are in agreement with results which illustrated that the cancer incidence and mortality is associated with low levels of ascorbic acid.(22) We can speculate that this protective effect may occur through antioxidant pathways or through enhancement of immune function. (21) There is also some recent evidence suggesting that ascorbate exerts a selective cytotoxic effect against malignant cells; all these observations indicate that supplemental ascorbate should be of some therapeutic value in the treatment of cancer.(22)

Table 1 shows levels of vitamin D (3.46, 3.63 µg|ml) for AML, ACML compared with controls (4.73µg|ml). The reduction of vitamin D level in AML and CML is in agreement with Drake, MT, Maurer MJ(23). Numerous epidemiological and preclinical studies support a role of vitamin D compounds in cancer prevention and treatment in colorectal, breast, prostate, ovarian, bladder, lung and skin cancers and leukemia(24).The newly recognized use of 1,25(OH)2D3 analogues as immunomodulatory agents is based on the ability of these analogues to influence gene expression in cells of the immune system and cytokine expression by other cells(25). In addition some non traditional roles ascribed to vitamin D include anti-flammatory and immune-modulating effects. (26)

Table 2 (opposite page) shows the results of cobalt, Nickel and magnesium, levels in sera of controls, AML and CML groups. The result of cobalt level in serum of patients with AML, CML, were (0.012 58 , 0.0154 ug/l), respectively, which are lower than serum level of controls (0.027930 ug/l). This result is in agreement with published results (0.03 ug/l) (27). It appears that the depletion of Cobalt in serum of patients is related to vitamin B12. (15) In addition, biological research that has been done suggests a relationship between cobalt and cancer(28).

The Nickel level in serum of patients with Acute CML were 0.01163 and 0.01390 respectively, which is lower than level in serum of controls, (0.01445 ug/l). This result is compared with Nickel level of patients and controls with published values (0.3 ug/l) (29, 15). In another study, high serum concentration of Nickel causes cancer because itdamages the chromosomes , and on a molecular basis Nickel induces DNA damage (DNA strand breaks and crosslink's infidelity of DNA replication, inhibition of DNA repair, and the helical of B-DNA to Z-DNA) by binding Nickel to the nuclear protein (30). These events reflected the effects of Nickel in two states of concentrations, in the statement of exposure to and the statement of lower levels, tended to cause cancer (31).

The Mg level in patient groups is significantly lower than controls. The decrease in Mg concentration in the many

Table 1: Serum concentration (µg|ml) of vitamin C and D in AML, CML and healthy control group.

Vitamin Groups	Vitamin C concentration µg|ml Mean ± SD	Vitamin D concentration µg|ml Mean ± SD	P
Healthy group N =35	4.2±2.0	4.73±2.11	
AML N = 22	3. 06±1.01	3.46±1.21	P<0.05
CML N = 20	3.46±1.21	3. 63±1.40	P<0.05

Table 2: The serum concentration(µg|l) of CO, Ni and Mg in AML, CML and healthy control group

Trace element Groups	CO concentration µg|l Mean ± SD		Ni concentration µg|l Mean ± SD		Mg concentration µg|l Mean ± SD	P
Healthy control N=35	0.027930 ±0.011		0.01445±0.0090		40.8±15.4	
AML N= 22	0.01258±0.0054	P<0.05	0.0116302 ±0.0028	P<0.05	33.7±10.3	P<0.05
CML N=20	00154±0.0035	P<0.05	0.01389±0.00 65	P<0.05	34.6±11.7	P<0.05
P*		P*>0.05		P*>0.05		P*>0.05

P* value between AML and CML

studies suggests the diminished Mg due to the high ATP requirement of the leukemia since Mg is known to be an important part as a cofactor in most of the energy producing reactions(32).

Figure 1, Figure 2 and Table 3 (next 2 pages) show the correlation relation between vitamin D and CO, Ni in sera of AML, CML and healthy control group; positive correlation between vitamin D and CO, Ni in healthy control group with r values (0.987,0.799), positive correlation between vitamin D and CO in AML and CML with r values (0.980,0.970); positive correlation between vitamin D and Ni in AML and CML with r values (0.948, 0.870)

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Table 3: Correlation relation between Vitamin D and Co, Ni in AML, CML and healthy control group.

Trace element groups	*Co-Concentration µg/L Mean ±SD (P-value and r)*	*Ni-Concentration µg/L Mean ±SD (P-value and r)*	*Vit.D-Concentration µg/ml Mean ±SD*
Healthy n = 35	0.027930 ±0.011 (3.55×10^{-13}, 0.987355)	0.01445± 0.00090 (3.42×10^{-13}, 0.799952)	4.73± 2.11
AML N = 22	0.01258 ± 0.0054 (6.27×10^{-17}, 0.980622)	0.0116302 ± 0.0028 (6.22×10^{-17}, 0.948111)	3.46 ± 1.21
CML N = 20	0.0154 ± 0.0035 (2.71×10^{-14}, 0.973719)	0.01389± 0.0065 (2.7×10^{-14}, 0.870364)	3.63 ± 1.40

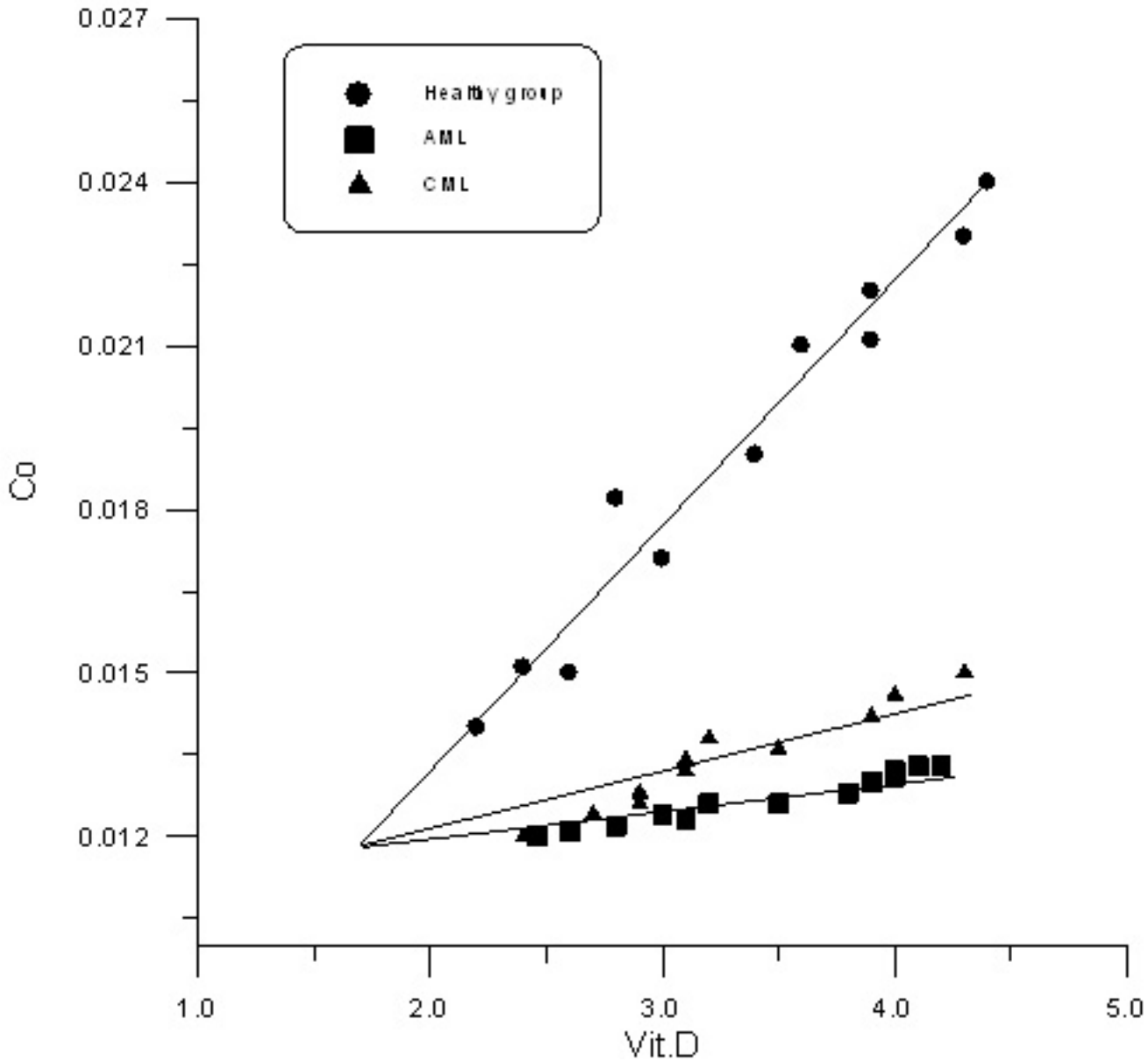

Figure 1

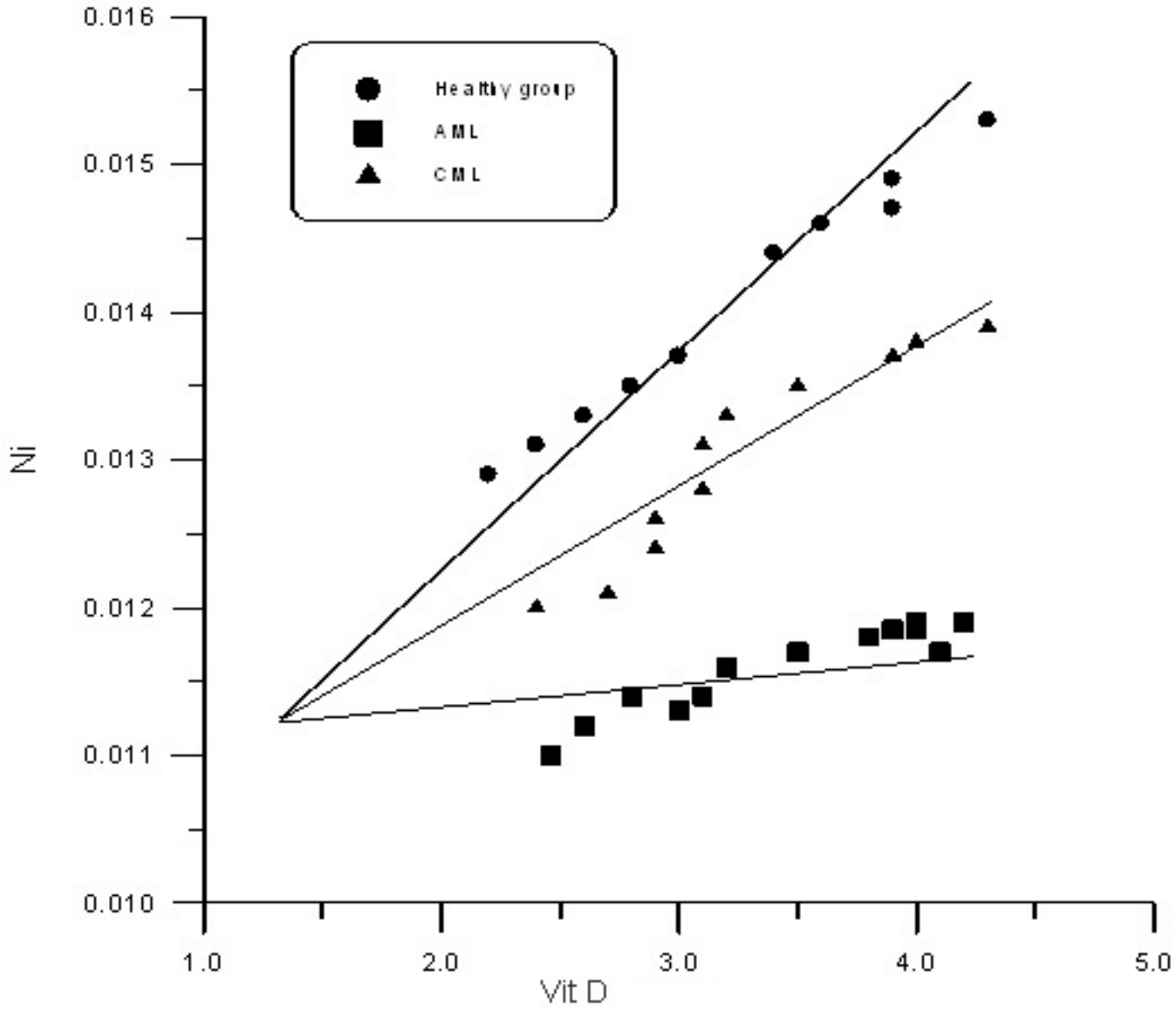

Figure 2

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