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Some endocrine hormones level associated with Chronic myelogenous leukemia patients in Al Anbar governorate

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ABSTRACT

Background and Objective: Leukemias are linked to numerous immunological and endocrine alterations. Numerous studies have demonstrated an association between endocrine hormone imbalance and the onset of disease in one or both sexes. Hormonal fluctuations can disrupt the physiological homogeneity of the human body, hence impacting health and the progression of associated disorders. We want to examine the impact of changes in endocrine hormones on the immunological response of persons with leukemia.

Materials and Methods: This case-control study enrolled 110 individuals, including 90 patients diagnosed with hematological malignancy, at the Medical City Department/Hematology Center in Baghdad, Iraq, from March to November 2024. Among 90 individuals diagnosed with leukemia, 70 were identified with sever chronic myeloid leukemia (CML1), whereas 20 were classed with moderate chronic myeloid leukemia (CML2) based on the disease duration. The research included 20 healthy participants as controls. Erythropoietin (EPO), homocysteine (THcy), parathyroid hormone (PTH), vitamin B12, vitamin D3, and folate levels were assessed in all individuals using both ELISA and immunofluorescence test methods. Calcitonin (Cal) and ferritin were also measured.

Results: The study's findings revealed a substantial increase in calcitonin (Cal) and ferritin levels ($P < 0.001$) in the experimental group compared to the control group. Serum Parathyroid hormone (PTH) levels were elevated in patients diagnosed with the CML1 and CML2 groups compared to the control group ($P = 0.01$). Erythropoietin (EPO) levels were significantly higher ($P = 0.02$) in both the CML1 and CML2 groups. The difference was shown to be statistically significant. Both CML1 and CML2 patients had significantly reduced levels of B12 and VD3 in comparison to the control group ($P = 0.01$ and 0.02, respectively). For Homocystine and Folate ($p = 0.004$, 0.001, respectively). he study's findings provide concrete evidence for the influence of hormones on the immune response in the etiology of leukemia.

Keywords: *Leukemia; endocrine hormones; Immune Response; Erythropoietin (EPO); Parathyroid hormone (PTH); Homocystine(THcy)*

1. INTRODUCTION

Hematologic cancer, another name for blood cancer, is a type of cancer that starts in tissues that generate blood, such as immune system cells and bone marrow. A variety of cancers, such as leukemia, lymphoma, and multiple myeloma, are included under blood cancer. Leukemia cells are abnormal white blood cells produced by the bone marrow in leukemia.[1]

Numerous physiological functions, including immunity, growth, reproduction, and metabolism, are regulated by hormones.[2] Leukemia is not officially categorized as a hormone-regulated hematological malignancy, despite the fact that its incidence and fatality rates are higher in men than in women [3]. Both males and females' treatment-free survival is

impacted differently by different levels of hormone exposure. Quantitative levels of PTH, calcitonin, EPO, vitamin B12, vitamin D3, folate, ferritin, and homocysteine (THcy) have all been studied. The median period of treatment-free survival was significantly shorter for males than for females.

An increasing amount of empirical data suggests that endocrine hormones and acute leukemia may be related [4]. Endocrine hormones use receptors that resemble those in differentiation factors like retinoids and are essential in controlling hematopoiesis. This connection may therefore be important for future research into the mechanisms governing leukemia growth control. Previous research has shown that most human leukemia cells have endocrine hormone receptors on their cellular surface, and that some subtypes of these cells proliferate more when endocrine hormones are present [6].

We examined the levels of endocrine hormones in patients with leukemia.

2. METHODOLOGY

Patients with hematological malignancies (acute and chronic leukemia) receiving treatment at the Al-Anbar Oncology Center ,in Al Anbar , Iraq, between March and November 2023 were the subjects of this case-control study. Senior medical professionals used patient histories, basic clinical features, and biochemical testing to diagnose the participants. There were two groups of 110 participants in the study. Twenty healthy people made up the control group, while 90 leukemia patients were divided into groups based on the length of their sickness, including 70 with CML1 (Group >1 y period) and 20 with CML2 (Group 1 y period). Every participant had blood drawn in order to assess PTH, calcitonin, EPO, vitamin B12, vitamin D3, folate, ferritin, and homocysteine (THcy). Age, sex, illnesses, and length of illness were all gathered from each subject's personal and medical history. Prior to blood collection, each research subject gave their informed consent. The subjects of each research group had a total of six milliliters of anticoagulated K3-EDTA blood drawn. After that, this blood was separated into milliliter pieces so that a thorough blood count could be performed. Centrifugation was used for 10 minutes at 4°C at a speed of 1006 Xg to separate the plasma from the remaining blood. The separated plasma was then kept at -20 degrees Celsius (-20 ˚C) to measure the levels of PTH, calcitonin, EPO, vitamin B12, vitamin D3, folate, ferritin, and homocysteine (THcy) using the Enzyme-Linked Immunosorbent Assay (ELISA) technique, in accordance with the manufacturer's instructions.

Statistical analysis

Two statistical metrics used to describe data are the mean and standard deviation (SD). The data's normality was evaluated using the Andersen-Darling test, which has a significance level of $P < 0.05$. The Student's t-test was used to evaluate the differences between the control and experimental subjects. To determine whether there were any statistically significant differences between the control group and the patient group, the researchers used a one-way analysis of variance (ANOVA). To assess the statistical significance, the ANOVA used Tukey's post hoc analysis. In every instance, the results' statistical significance was determined to be $P < 0.05$.

3. RESULTS

Ninety individuals with leukemia, 70 patients in Group CML1 (32 females and 38 males) with a mean age of 47.09 ± 4.07 years, and 20 patients in CML2 Group (7 females and 13 men) with a mean age of 41.90 ± 0.97 years comprised the 110 subjects that were included in the study. Additionally, 20 patients (9 females and 11 males) with an average age of 45.6 ± 2.7 years were enlisted as the control group; demographic estimates are shown in table 1.

Table 1. Demographic distribution of study participants

Groups	Control(n=20)	CML1(n=70)	CML2(n=20)
Sex	(F=9, M=11)	(F=32, M=38)	(F=7, M=13)
Mean age ±SD	45.6 ± 2.7	47.09 ± 4.07	41.90 ± 0.97
P Value	0.011	0.034	0.021

As shown in Table 2, the clinical and biochemical characteristics of leukemia patients were contrasted with those of a Control Group. Table 2 shows that patients in Group CML1 and Group CML2 had statistically significant increases ($P < 0.005$) in their serum levels of EPO and PTH compared to the Control Group. Ferritin levels in both leukemia groups (Groups CML1 and CML2) were found to be statistically significantly higher than those in the Control Group ($P = 0.001$, Table 2). Ferritin levels were also found to differ significantly between the two leukemia groups. The calcitonin levels in both leukemia groups were significantly higher than those in the control group ($P<0.001$). Table 2 shows that patients in Group CML1 and CML2 had significantly lower levels of B12 and VD3 than those in the Control Group ($P = 0.001, 0.002$, respectively). The results showed a statistically significant increase in homocystein ($P = 0.004$).

Furthermore, the results indicate that, in comparison to the control group, folate is considerably reduced in all patient groups (P = 0.001).

Table 2. Comparing the research groups' biochemical parameter

Parameters	CML1 Group	CML2 Group	Control Group	P Value
PTH	33 ± 4.6	52 ± 7.3	23 ± 4.27	0.001
calcitonin	387 ± 11.9	161 ± 4..12	80 ± 5.32	< 0.001
EPO	210 ± 2.60	112 ± 14.31	14.4± 1.0	0.002
B12	541 ± 10.72	317 ± 8.04	650± 78.90	0.01
D3	19 ± 3.92	28 ± 1.7	32 ± 3.70	0.02
Folate	14.2 ± 0.94	10.5 ± 3.05	16 ± 0.6	0.001
Ferritine	321 ± 10.07	68 ± 12.5	280 ± 22.6	0.001
Homocystien	10.11 ± 2.64	5.32 ± 0.76	3.3 ± 0.48	0.004

4. DISCUSSIONS

This investigation's findings show that Calcitonin and serum ferritin level are raised by 20.24 % and 15.37 % respectively in persons belonging to Groups CML1 and CML2 in comparison to Control Group (P < 0.05). However, there were seemingly large differences in terms of ferritin in the different patient-groups. This observation is in consonant with the findings made by Toro-Tobón et al. [7] and Larrue et al [8] in different studies that they undertook.

The present study confirmed the data of Angenendt et al[9] that showed the increase of calcitonin concentration in blood of patients with acute leukemia and generation of this hormone by leukemic blasts. Elevated circulating calcitonin-related peptides and overall increased prevalence of risk factors in acute leukemia patients were compared to clinical outcomes in 77 patients.

A statistically significant elevation of EPO was noted in both subgroups of the examined leukemia patients compared to the control group (P < 0.05).

The analyzed data show an outcome with increased PTH measurement with Groups CML1 and CML2 in comparison to the control group with a probability level less than 0.05. Finally, it is noticeably seen that the patients have a way better outcome than the control group.

The levels of EPO are significantly higher in the current study meaning increased erythroid lineage precursors developed from EPO and circulating granulocyte-macrophage colony-forming units [10]. Hussein et al. [11] and Cesini et al. [12] present evidence of Epo promoting the development of acute leukaemia: In their in vitro simulation experiments of myeloblastic cells obtained from patients with acute leukemia, it was. The individual administration of Epo did not support the development of leukemic blast colonies, but if they are administered with colony stimulating substances, there would be a significant increase in the number of leukemic blast colonies. The proliferative response was not confined to erythroid lineage but also acute leukemia blast Epo [13].

Thus, the present study result shows that all the patients of CML1 and CML2 presented significantly low level of VD3 as compared to the control group. However, the differences attained in the levels of VD3 were considered highly very significant with regard to leukemia patents and the normal group.

In the course of this study it was possible to prove reduced serum B12 in Group CML1 and CML2 as compare to the control group in Statistical analysis (P < 0.05). But as for patient's groups, the increase of B12 concentration pre and post intervention could not be revealed.

The writers of the current study are not alone in having proposed the utilization of Vitamin D3 and B12, following studies made by Atoum et al.[14] In the past, Vitamin D3 and B12 are known to be special antiviral agents. Most commonly, they go through controlled growth and division according to the necessity that is identified within the body. Patients having leukemia experience such scenario where the bone marrow releases low levels of reborn incorrect VD3 and B12. It changes the morphologies of these cells according to the leukemia microenvironment, neutrophils polarized into the leukemia

combatant.[15].

Low serum levels of vitamin D3 and B12 in patients with acute lymphoblastic leukemia means poor clinical condition and prognosis[16]..Endocrine hormones regulate secretion, metabolism, growth and development. It is also noteworthy that no parallel cause and effect relationship between leukemia and B12 and VD3 presence were indicated, however, certain factors linked with the development of leukemia as well as its treatment may definitely have an impact.[17].

Ferritin is an iron storage protein, and it is synthesized through the mammalian metabolic system. However, it is also classified as an acute phase protein. High levels of serum ferritin can indicate an existing health condition like certain types of cancer, in which causes increased deposition of iron in the body.[18] Overt or subclinical inflammation may increase baseline levels in all the probably patients. This signal may trigger a pathophysiological examination aimed at identifying a potentially pathogenic inflammation. In addition, it may represent the potential using higher or modified immune therapies in the future. Cancer patients have higher blood ferritin concentrations that are characteristic of increased synthesis of this protein by macrophages. It has been documented that hepcidin enables iron to be taken up by macrophages when there are inflammatory events[19]. Another study implies that high serum ferritin level is due to the activation of transferrin receptors on leukemic clones of malignant nature. Furthermore, high level of cell turnover suggests the transport of ferritin and raises the serum levels, facts which are in concordance with Albert and Schmidt's observations.[20]. Our data shows that PTH are normal levels; hypercalcemia in leukemia is due to direct invasion of bones by tumor cells, ectopic production of PTH or cytokines stimulating bone resorption. This conclusion supports Kohart [21], in which the author described the case of a 51-year-old man presenting back pain, circulating myeloblast, and hypercalcemia. These included acute myeloblastic leukemia as showed by the results of the bone marrow. The levels of the parathyroid hormone and PTH related peptide were either normal or subnormal. In the specimen histomorphometry, cortical thinning was observed, and some of the intracortical erosion voids present extended into the region of the marrow.

The results pointed that the level of folate has decreased; a large number of works have been devoted to the study of serum levels of folate and the dynamics of Figlu in patients with leukemia. They concluded that folate deficiency is an emerging factor linked to these disorders [22] , [23].

Based on our findings, homocysteine levels seem to be raised; deranged homocysteine metabolism ties numerous human cancers, most of which belong to leukemia. Many studies focus different aspects of genetics, epigenetics, and the environment concerned possible causes associated with homocysteine metabolism and cancer. In a specific manner, low folate (vitamin B9) reduces homocysteine or vice versa. Further study may discover information that can allow for new treatments regarding cancer, as well as methods of detecting cancer[24] and [25].

5. CONCLUSION

The initial outcome of the present study is that above mentioned disease has a direct effect on

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