Ministry of Planning

Central Organization for Standardization and Quality Control

Directorate of Patents and Industrial Models

The impact of Reproductive Hormone changes on the immune response in leukemia patients, including workers in chemical laboratories

Dr.JINAN AZEEZ THABET

2024

The impact of Reproductive Hormone changes on the immune response in leukemia patients, including workers in chemical laboratories

Dr. Jinan Azeez Thabit

Directorate of Patents and Industrial Models, Central Organization for Standardization and Control Quality, Ministry of Planning, Al Jadryia St., Baghdad, Iraq

LIST OF CONTENTS

Contents

Study framework:

This study employed a case-control design and focused on patients diagnosed with hematological cancer (specifically acute and chronic leukemia) who were treated at the Medical City Department/Hematology Center in Baghdad, Iraq. Information regarding individuals' ages, genders, genetic profiles, and body mass indices was gathered, from February 2022 to October 2022.

Objective of the study:

The objective of this study was to investigate the influence of alterations in reproductive hormones on the immune response of individuals diagnosed with leukemia.

The impact of Reproductive Hormone changes on the immune response in leukemia patients for workers in chemical laboratories

Dr. Jinan Azeez Thabit

Abstract

Background: Leukemias are associated with immune and endocrine changes. Several studies have established a correlation between an imbalance in pituitary hormones and sex steroids and the initiation of illness in either one or both genders. The objective of this study was to investigate the influence of alterations in reproductive hormones on the immune response of individuals diagnosed with leukemia.

Methods: A total of 130 subjects were enrolled in the study, comprising 80 patients diagnosed with leukemia, 45 patients diagnosed with acute myeloid leukemia (AML), and 35 patients diagnosed with acute lymphoblastic leukemia (ALL). The study involved 50 healthy controls. Estradiol (E2), triiodothyronine (T3), follicle-stimulating hormone (FSH), and progesterone levels were measured using both ELISA and the immunofluorescence assay method.

Results: The findings of the study demonstrated a significant elevation in the levels of C-reactive protein (CRP), ferritin, and neutrophil-to-lymphocyte ratio (NLR) in the patient group when compared to the control group. Serum progesterone is increased in patients diagnosed with AML and ALL in comparison to the control group. FSH was elevated in AML

and decreased in ALL. This difference was found to be statistically significant. The levels of E2 and T3 were found to be significantly reduced in both AML and ALL patients when compared to the control group.

Conclusions: The findings of the study offer empirical support for the impact of hormones on the immune response in leukemia pathogenesis.

Keywords**:** acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), Estradiol, immune response, and triiodothyronine (T3).

Introduction

Blood cancer, also known as hematologic cancer, is a malignancy originating from blood-forming tissues, including the bone marrow and immune system cells. Blood cancer encompasses various types of malignancies, including leukemia, lymphoma, and multiple myeloma. When an individual is afflicted with Leukemia, their bone marrow generates atypical white blood cells, referred to as leukemia cells (1).The stem cells located in the anterior pituitary are responsible for differentiating into distinct cell types that secrete various hormones, such as adrenocorticotropic hormone (ACTH), growth hormone (GH), prolactin, thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH). The tropic hormones exert control over various physiological processes such as immunity, growth, reproduction, and metabolism(2).Despite the higher incidence and mortality rates of leukemia in males compared to females, this hematological malignancy is not currently classified as hormone-regulated. Diverse levels of hormonal exposure are associated with varying effects on treatment-free survival in both males and females. studies examined the quantitative concentrations of progesterone, adrenal precursors, androgens, estrogens, catechol estrogens, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). The treatment-free survival median for males was comparatively shorter in duration when compared to that of females. The hormonal profiles exhibited by the patients in the studies were markedly distinct from those observed in the control group comprising of healthy volunteers. The duration of treatment-free survival in male patients was found to be

significantly extended in cases where LH levels were observed to be lower. Several studies have established a correlation between an imbalance in pituitary hormones and sex steroids and the initiation of illness in either one or both genders (3).Numerous in vitro studies have demonstrated an association between sex hormones and leukemia. The challenge of providing a comprehensive explanation for this correlation is further complicated by the contradictory findings observed in other related studies (4).The steroid sex hormones exert an influence on leukemias and lymphomas that are determined by sexual characteristics. Males may exhibit increased vulnerability to developing ALL due to diminished levels of estrogen compared to females (5).The occurrence of tumor growth and metastasis in humans has been associated with a range of endocrine systems, including those that govern reproductive functions. Extensive documentation exists regarding the correlation between prenatal exposure to exogenous hormones and an increased susceptibility to cancer in offspring. A limited number of studies have demonstrated a heightened occurrence of fetal Leukemia in cases where women utilize hormonal contraceptives (6).Sex steroids belong to one of two families of nuclear receptors. The primary group encompasses receptors for the hormones androgen, estrogen (E2), progesterone, glucocorticoids, and mineralocorticoid (MR). The role of ligands for these receptors in the proliferation and differentiation of various cell lineages in normal hematopoietic tissue is widely acknowledged. This also extends to their impact on myeloid cancer cells (7).The identification of ER expression in chronic lymphocytic leukemia (CLL) indicates the presence of a cell subpopulation in this malignancy that is influenced by hormones(8).A growing body of empirical evidence indicates a potential association

between autoimmune thyroid disease and acute leukemia. Thyroid hormones play a crucial role in regulating hematopoiesis and utilize receptors that bear resemblance to those found in differentiation factors such as retinoids. Consequently, this association holds potential significance for further investigations into the mechanisms underlying growth control in leukemia(9).The occurrence of low T3 syndrome is common among patients who are admitted to critical care units due to severe illnesses, including pneumonia, Hodgkin's disease, and chronic lymphocytic leukemia(10).Certain subtypes of human leukemia cells exhibit an augmented proliferation in the presence of growth hormone (GH), and previous studies have demonstrated the prevalence of growth hormone receptor (GHR) on the cellular surface of the majority of these cells(11).The study aimed to examine the impact of reproductive hormones changes on immune response of patients with leukemia.

Subjects and Methods

Subjects

This study employed a case-control design and focused on patients diagnosed with hematological cancer (specifically acute and chronic leukemia) who were treated at the Medical City Department/Hematology Center in Baghdad, Iraq. A total of 130 subjects were included in the study, consisting of 80 patients diagnosed with leukemia, 45 patients diagnosed with AML (19 females and 26 males), with a mean age of (32.32±2.69),

Additionally, there were 35 patients diagnosed with ALL (16 females and 19 males), with a mean age of (35.794±0.63). Blood samples were collected from all subjects for analysis. The study included a total of 50 individuals who were deemed healthy and served as the control group. Among these participants, 28 were female and 22 were male. The average age of the control group was (41.8±1.57) years. Participant diagnoses are determined by senior medical professionals through the analysis of fundamental clinical features, patient histories, and biochemical testing. Information regarding individuals' ages, genders, genetic profiles, and body mass indices was gathered.

Methods

A total of six milliliters of anticoagulated K3-EDTA blood were collected from each research group's subjects. This blood was then divided into one milliliter portions for the purpose of conducting a Complete Blood Count. Plasma was isolated from the rest of the blood through centrifugation at a speed of 1006 Xg for 10 minutes at a temperature of 4°C. The separated plasma was subsequently stored at a temperature of negative 20 degrees Celsius (-20 ˚C) for the purpose of assessing E2 levels using the Enzyme-Linked Immunosorbent Assay (ELISA) technique. Additionally, T3, FSH, and Progesterone levels were determined using the immunofluorescence assay method as per the instructions provided by the manufacturer. Furthermore, the concentration of C-reactive protein (CRP) was also determined.

Statistical analysis

The mean and standard deviation (SD) are statistical measures employed to characterize data. The Andersen-Darling test was employed to assess the normality of the data, with a significance level of $p \leq 0.05$. The

distinction between control and experimental subjects was assessed using Student's t-test. The researchers employed a one-way analysis of variance (ANOVA) to examine whether there were any statistically significant differences between the control group and the group of patients. Tukey's post hoc analysis was employed in the ANOVA to evaluate the statistical significance. The statistical significance of the results was established when the *p*-value was found to be less than 0.05 in all cases.

Results

The clinical and biochemical variables of patients diagnosed with leukemia were compared to those of a control group, as presented in Table 1. The serum levels of CRP exhibited a statistically significant increase ($p \leq 0.05$) in patients diagnosed with AML and ALL when compared to the control group, as indicated in Table 1. The results indicate a statistically significant increase in ferritin levels in both leukemia patient groups (AML and ALL) when compared to the control group ($p \leq 0.05$, Table 1). Additionally, a significant difference in ferritin levels was observed between the two patient groups.

Table 1: Comparison of the biochemical parameters in study groups.

Parameters (Mean± SD)	**Groups**			
	Patients with leukemia		**Control**	***p*-value**
	AML n=45	**ALL n=35**	**n=50**	
CRP (mg/l)	**216.05±31.6 [b]**	**133.78±4.45 [a]**	**4.13±1.79[a]**	**$p \leq 0.05$**
Ferritin (ng/ml)	**327.86±26.82 [b]**	**269.03±8.33 [c]**	**84±34.055[a]**	**$p < 0.05$**

CRP: C-reactive protein. A one-way ANOVA test was used to validate the data. Different letters indicted statistically significance.

There was a notable rise observed in white blood cell (WBC) counts in both groups of patients when compared to the control group ($p \leq 0.05$). A notable reduction in neutrophil counts was observed among patients diagnosed with AML in comparison to the control group ($p \leq 0.05$) while insignificant alterations were noted in patients with ALL, as depicted in Table 2. The findings indicated that there were no statistically significant alterations in lymphocyte counts ($p \geq 0.05$). Additionally, the findings suggest that the neutrophil-to-lymphocyte ratio (NLR) is significantly elevated in all groups of patients when compared to the control group ($p \leq 0.05$).

Table 2: WBC, Neutrophil count, Lymphocytes count and NLR, expressed as mean ± SEM, in patient groups and control

Parameter/Group	**AML**	**ALL**	**Control**	***p*-value**
WBC	**11.58±3.99 [b]**	**27.25±2.06 [c]**	**7.57±0.16 [a]**	**≤0.05**
Neutrophil count	**37.43±4.68 [b]**	**41.16±6.78 [a]**	**56.75±13.22 [a]**	**≤0.05**
Lymphocyte count	**28.08±4.21 [a]**	**24.19±1.51 [a]**	**30.89±1.04 [a]**	**≥0.05**
NLR	**3.16±0.66 [b]**	**6.26±0.51 [c]**	**1.90± 0.06 [a]**	**≤0.05**

** A one-way ANOVA test was used to validate the data. Different letters indicted a statistically significance*

The levels of progesterone, FSH, and T3 were quantified using the immunofluorescence assay method in both leukemia patients and control groups. There was a significant increase in progesterone levels observed in both AML and ALL patients when compared to the control group ($p \leq 0.05$) (Table 3). There was a notable rise in FSH levels among individuals diagnosed with AML in comparison to the control group. Conversely, patients with ALL exhibited a decrease in FSH levels. This difference was statistically significant ($p \leq 0.05$). The findings demonstrated a statistically significant reduction in T3 levels among all patients diagnosed with AML and ALL in comparison to the control group ($p \leq 0.05$). Significant differences were observed in leukemia patients compared to the control group, as indicated by the statistical analysis ($p \leq 0.05$, Table 3-4). The levels of E2 were found to be significantly lower in both AML and ALL patients when compared to the control group ($p \leq 0.05$).

Table 3: The levels of progesterone, FSH, T3 and E2 in study groups

Parameters Mean ± MD	**Study Groups**		**Control**	***p*-value**
	AML	**ALL**		
Progesterone (ng/ml)	**6.625±2.281 [b]**	**6.90±2.16[b]**	**2.96±1.58[a]**	**≤0.05**
FSH (mlU/ml)	**9.26±3.73[b]**	**2.86 ±1.50[c]**	**6.21±1.79 [a]**	**≤0.05**
T3 (ng/ml)	**0.58±0.18 [b]**	**0.52±0.133[b]**	**1.29±0.38 [a]**	**≤0.05**
E2 (pg/ml)	**251.72±10.06[b]**	**245.99±8.82[b]**	**445.22±39.93[a]**	**≤0.05**

Discussion

The primary characteristic of Leukemia is the unregulated accumulation of blood cells, which may include malignant cells. While it is true that males have a higher likelihood of being diagnosed with and succumbing to Leukemia compared to females, it is important to note that this particular form of blood cancer is not currently classified as hormone-regulated.

The results of this investigation demonstrate a statistically significant increase in the levels of CRP in the serum of individuals who have been diagnosed with AML and ALL in comparison to the control group ($p \leq 0.05$).

CRP is a type of acute-phase protein that is synthesized in the liver as a result of cytokine stimulation, specifically interleukin-6 (IL-6) signaling. CRP plays a crucial role in modulating the inflammatory response through its ability to enhance the functionality of phagocytes and initiate the activation of the complement system. The study conducted by researchers revealed that individuals diagnosed with various types of cancer, including hematologic malignancies, exhibited lower rates of survival when their levels of CRP were elevated (12).A highly sensitive c-reactive protein in AML, when compared with a control group, is in agreement with this study (13), The elevation of CRP levels in patients can be attributed to various factors, such as the body's reaction to tumor necrosis, localized tissue damage, or concurrent inflammation (14).Proteins such as CRP are involved in the systemic inflammatory response associated with cancer. CRP serves as an indicator of inflammation and nutritional status, and has shown potential as a prognostic factor for predicting the survival of leukemia patients and other

types of cancer(15).Ferritin is a protein synthesized through mammalian metabolic processes, primarily serving as a means to store iron within tissues. Additionally, it is classified as an acute phase protein. Elevated blood ferritin levels may indicate the presence of an underlying medical condition, such as specific types of cancer, which can lead to excessive iron accumulation within the body(16).The current investigation demonstrated a statistically significant elevation in serum ferritin levels among both groups of leukemia patients (AML and ALL) when compared to the control group ($p \leq 0.05$). Furthermore, it is worth noting that there exists a substantial disparity in ferritin levels among the different groups of patients. This finding aligns with the conclusions drawn by Mosab and Fang Wang *et al*. in their respective studies (17,18). Overt and subclinical inflammation may induce higher baseline levels in all patients(19). Furthermore, it is possible that this marker could serve as a prompt for conducting a diagnostic workup to identify any underlying pathological inflammation. Additionally, it may indicate the potential advantages of utilizing augmented or targeted immune interventions(20). Moreover, it has been observed that individuals diagnosed with cancer exhibit elevated levels of blood ferritin, a phenomenon that has been linked to an increased production of this protein by macrophages. The role of hepcidin in promoting iron uptake by macrophages during inflammatory processes has been documented(21).Another study indicates elevated serum ferritin levels due to elevated transferrin receptors on malignant clones of leukemic cells. Additionally, high cell destruction rates reveal ferritin carriage and raise serum levels, which are also consistent with the study's results by Albert and Schmidt (22). There was a notable rise in WBCs counts observed in both groups of patients with leukemia in comparison to the

control group ($p \leq 0.05$). Based on previous studies conducted by Sameh and Rudresha *et al*. (23,24), WBCs are highly effective combatants against infections. Typically, they undergo controlled growth and division in accordance with the body's requirements. However, individuals diagnosed with leukemia experience a condition where the bone marrow overproduces an excessive number of abnormal WBCs that exhibit impaired functionality. The phenotypes of these cells are influenced by the leukemia microenvironment, resulting in the polarization of neutrophils into cells that combat leukemia (25). Progesterone is an essential hormone that plays a crucial role in maintaining overall health by modulating the immune response in various disorders, including autoimmune, infectious, and malignant conditions. This modulation occurs through its influence on both the innate and adaptive immune systems(26). The current findings demonstrate a significant increase in progesterone levels among patients diagnosed with AML and ALL when compared to the control group ($p \leq 0.05$). The patients exhibited a more pronounced effect in comparison to the control group. Research studies have demonstrated a notable enhancement in immune system functionality as a result of the administration of the hormone progesterone. This proposed mechanism suggests that the suppression of infection with microorganisms and the subsequent adaptive inflammatory response may be achieved through the administration of progesterone at significantly elevated levels. This has the potential to be a unique focus not only in the field of cancer therapeutics but also in the management of inflammatory and autoimmune diseases (27–30). In contrast, the utilization of oral medications containing a combination of estrogen and progestin has been associated with an increased risk of leukemia(31,32).Chemotherapy has the potential to

disrupt hormonal equilibrium, albeit without a direct correlation to the presence of leukemia. Generally, hormone levels remain unaffected until the disease has advanced to the glands responsible for hormone production or unless the treatment for leukemia directly affects these glands (33,34). Patients with AML exhibited a notable elevation in FSH levels, whereas patients with ALL demonstrated a decrease in FSH levels when compared to the control group ($p \leq 0.05$). This finding aligns with the findings of a study conducted by Huina *et al.*(35). which found the hypogonadism secondary to antineoplastic treatment (characterized by elevated levels of LH and FSH owing to the lack of negative feedback from the gonads). Another research by Mohammad *et al.*(36) showed that cancer could impair fertility directly by affecting reproductive organs and indirectly by inhibiting reproductive function or delaying reproduction due to cancer treatment.

The primary role of FSH is to regulate the reproductive system. Certain therapies for leukemia have the potential to indirectly affect FSH levels. This can occur through the detrimental effects on the ovaries or testicles, which subsequently influence the production of hormones by these organs(37). The findings demonstrated a statistically significant reduction in T3 levels among all patients diagnosed with AML and ALL when compared to the control group. Moreover, the changes observed in T3 levels were found to be highly significant in leukemia patients compared to the control group. Patients with ALL who have low serum T3 levels demonstrate a negative clinical status and prognosis ALL(38).Thyroid hormones (T3 and T4) are crucially involved in the processes of metabolism, growth, and development. Although there is no direct causal link between leukemia and low levels of T3, various factors

related to leukemia and its treatment have been found to potentially impact thyroid hormones levels, resulting in a decrease in T3 levels. The exact mechanisms underlying the phenomenon of low T3 have not yet been completely understood. The involvement of multiple cytokines, particularly in patients with hematological malignancies who are critically ill, and the subsequent upregulation of various cytokines, hinder the synthesis of thyroid hormones, indicating a systemic inflammatory response in cancer patients with elevated levels of C-reactive protein CRP(38).There were notable and statistically significant differences observed in leukemia patients when compared to the control group(39). According to research done by Salvatore *et al*. (40). The study demonstrated a correlation between decreased levels of T3 serum and an increased Absolute Neutrophil Count, indicating that alterations in IL-6, IP-10, and MCAF are the main factors influencing T3 serum levels, particularly in patients with coexisting hematological malignancies. A potential indicator for prognostic evaluation in future clinical applications of leukemia could be the presence of low levels of T3 (41).The findings of the study indicated a statistically significant decrease in serum E2 levels among patients diagnosed with AML and ALL compared to the control group ($p \leq 0.05$). However, no significant alterations in E2 levels were observed within the patient groups themselves. This statement is in accordance with the findings of Samir *et al*.(42), who Serum E2 levels were quantified in patients with acute leukemia, and the potential diagnostic value of these levels was extrapolated in a clinical context. Furthermore, it is worth noting that estrogen deficiency is associated with significant alterations in bone marrow hematopoiesis, leading to the inhibition of stem cell

differentiation into myeloid and lymphoid lineages(43).E2 is subject to the influence of various variables, including age, the menstrual cycle, pregnancy, and specific medical conditions. The relationship between blood levels of E2 and leukemia lacks conclusive evidence. Some chemotherapy medications have the potential to induce testicular or ovarian failure in both males and females, leading to potential alterations in the levels of E2(44).

Conclusions

The main findings of the current study indicate that patients with leukemia exhibited elevated levels of CRP, ferritin, and NLR. These increases can be attributed to the augmentation of pro-inflammatory reactions and a deficiency in the regulation of anti-inflammatory responses. The presence of irregular hormone levels, specifically heightened progesterone and FSH, alongside diminished T3 and E2 levels, may have an impact on the immune response of individuals with leukemia. This observation has the potential to provide novel insights into the development of strategic therapeutic approaches for leukemia.

Recommendations

Measurement of mitochondrial NADH dehydrogenase 1 activity and mRNA expression in leukemia, which may be associated with risk of leukemia and in the prediction for it.

References:

1. Mohamed H, Omar R, Saeed N, Essam A, Ayman N, Mohiy T, et al. Automated detection of white blood cells cancer diseases. Proc IWDRL 2018 2018 1st Int Work Deep Represent Learn. 2018;(March):48–54.

2. Tomida M, Yoshida U, Mogi C, Maruyama M, Goda H, Hatta Y, et al. Leukaemia inhibitory factor and interleukin 6 inhibit secretion of prolactin and growth hormone by rat pituitary MtT/SM cells. Cytokine. 2001;14(4):202–7.

3. Allain EP, Venzl K, Caron P, Turcotte V, Simonyan D, Gruber M, et al. Sex-dependent association of circulating sex steroids and pituitary hormones with treatment-free survival in chronic lymphocytic leukemia patients. Ann Hematol. 2018;97(9):1649–61.

4. Scandinsrica M. Sex Horiiiones and Leukemia .’. 1948;CXXXII.

5. Ben-Batalla I, Vargas-Delgado ME, Meier L, Loges S. Sexual dimorphism in solid and hematological malignancies. Semin Immunopathol. 2019;41(2):251–63.

6. Blethen SL. Leukemia in children treated with growth hormone. Trends Endocrinol Metab. 1998;9(9):367–70.

7. Mossuz P, Cousin F, Castinel A, Chauvet M, Sotto MF, Polack B, et al. Effects of two sex steroids (17β estradiol and testosterone) on proliferation and clonal growth of the human monoblastic leukemia cell line, U937. Leuk Res. 1998;22(11):1063–72.

8. Gordon I, Epstein L, Lb- E, Lb- E. in Chronic. 1983;62(5):996–9.

9. Moskowitz C, Dutcher JP, Wiernik PH. Association of thyroid disease with acute leukemia. Am J Hematol. 1992;39(2):102–7.

10. Sciacchitano S, De Vitis C, D'Ascanio M, Giovagnoli S, De Dominicis C, Laghi A, et al. Gene signature and immune cell profiling by high-dimensional, single-cell analysis in COVID-19 patients, presenting Low T3 syndrome and coexistent hematological malignancies. J Transl Med [Internet]. 2021;19(1):1–20. Available from: https://doi.org/10.1186/s12967-021-02805-6

11. Manabe N, Kubota Y, Kitanaka A, Ohnishi H, Taminato T, Tanaka T. Src transduces signaling via growth hormone (GH)-activated GH receptor (GHR) tyrosine-phosphorylating GHR and STAT5 in human leukemia cells. Leuk Res. 2006;30(11):1391–8.

12. Yang X, Yin H, Xiao C, Li R, Liu Y. The Prognostic Significance of C-Reactive Protein to Albumin Ratio in Patients With Severe Fever With Thrombocytopenia Syndrome. Front Med. 2022;9(January):303–16.

13. Amin MN, Permatasari N. The Role of Stem Cell on Orthodontic Tooth Movement Induced-Alveolar Bone Remodeling. Res J Pharm Technol. 2023;16(1):123–8.

14. Iqbal A, Zaid M, Munir R, Usman H, Kalbacher H, Scandiuzzi L, et al. Clinica Chimica Acta Atypical plasma lipid pro fi les in leukemia. 2016;452:129–33.

15. Tang HN, Pan BH, Wang L, Zhu HY, Fan L, Xu W, et al. C-reactive protein-to-albumin ratio is an independent poor prognostic factor in

newly diagnosed chronic lymphocytic leukaemia: A clinical analysis of 322 cases. Transl Oncol [Internet]. 2021;14(4):101035. Available from: https://doi.org/10.1016/j.tranon.2021.101035

16. Guidelines. B. High Ferritin and Iron Overload – Investigation and Management. BC Guidel. 2021;1–16.

17. Nouraldein M, Hamad M. Assessment of Serum Ferritin Levels in Sudanese Patients with Acute Lymphoblastic Leukemia. Int J Med Res Heal Sci [Internet]. 2019;8(7):92–6. Available from: www.ijmrhs.com

18. Wang F, Lv H, Zhao B, Zhou L, Wang S, Luo J, et al. 铁与白血病：未来治疗的新见解. J Exp Clin Cancer Res. 2019;38:1–17.

19. Ihlow J, Gross S, Sick A, Schneider T, Flörcken A, Burmeister T, et al. AML: high serum ferritin at initial diagnosis has a negative impact on long-term survival. Leuk Lymphoma. 2019;60(1):69–77.

20. Jain P, Casteel K, Allen CE, McClain KL, Wang S, Konoplev S, et al. Elevated Ferritin Predicts for Inferior Survival in Patients with Acute Leukemia and May be an Early Marker of a Underlying Systemic Pathologic Inflammation. Blood [Internet]. 2016;128(22):2791–2791. Available from: http://dx.doi.org/10.1182/blood.V128.22.2791.2791

21. George A, Bobby Z, Dubashi B. Utility of ferritin and inflammatory biomarkers in the diagnosis of different stages of breast cancer. Saudi Med J. 2021;42(8):825–31.

22. Aulbert E, Schmidt CG. Ferritin--a tumor marker in myeloid

leukemia. Cancer Detect Prev. 1985;8(1–2):297–302.

23. Abd El-Ghany S, Elmogy M, El-Aziz A. Computer-Aided Diagnosis System for Blood Diseases Using EfficientNet-B3 Based on a Dynamic Learning Algorithm. Diagnostics. 2023;13(3).

24. Antapura RH, Vaibhav AB, Dasappa L, Jacob LA, Sureshbabu MC, Lokesh KN, et al. Adult Philadelphia-Positive Acute Lymphoblastic Leukemia: A Single-Institution Experience in Limited-Resource Setting. South Asian J Cancer. 2023;

25. Jegal Y. The role of neutrophils in the pathogenesis of IPF. Korean J Intern Med. 2022;37(5):945–6.

26. Shah NM, Lai PF, Imami N, Johnson MR. Progesterone-related immune modulation of pregnancy and labor. Front Endocrinol (Lausanne). 2019;10(MAR):1–19.

27. Srivastava MD, Thomas A, Srivastava BIS, Check JH. Expression and modulation of progesterone induced blocking factor (PIBF) and innate immune factors in human leukemia cell lines by progesterone and mifepristone. Leuk Lymphoma. 2007;48(8):1610–7.

28. Check JH, Check DL. The role of progesterone and the progesterone receptor in cancer: progress in the last 5 years. Expert Rev Endocrinol Metab. 2023;(just-accepted).

29. Aganezov SS, Ellinidi VN, Morotskaya A V, Artemyeva AS, Nyuganen AO, Aganezova N V. Endometrial expression of leukemia inhibitory factor in women with different estrogen/progesterone receptor status of the endometrium. Obstet Gynecol Reprod. 2019;13(2):85–94.

30. Xiong Y, Wang Y, Ma L, Zhang Y, Qu X, Huang L, et al. Mixed-lineage leukaemia 1 contributes to endometrial stromal cells progesterone responsiveness during decidualization. J Cell Mol Med. 2021;25(1):297–308.

31. Hargreave M, Mørch LS, Andersen KK, Winther JF, Schmiegelow K, Kjaer SK. Maternal use of hormonal contraception and risk of childhood leukaemia: a nationwide, population-based cohort study. Lancet Oncol. 2018;19(10):1307–14.

32. Tauchmanovà L, Selleri C, De Rosa G, Sammartino A, Di Carlo C, Musella T, et al. Estrogen-progestin therapy in women after stem cell transplant: Our experience and literature review. Menopause. 2007;14(2):320–30.

33. Nieman LK. Molecular Derangements and the Diagnosis of ACTH-Dependent Cushing's Syndrome. Endocr Rev. 2022;43(5):852–77.

34. Samimi A, Ghanavat M, Shahrabi S, Azizidoost S, Saki N. Role of bone marrow adipocytes in leukemia and chemotherapy challenges. Cell Mol Life Sci. 2019;76:2489–97.

35. Su H, Zhou X, Zhao Y, Lu Y, Liu DY, Zhang J, et al. Gynecological complications in long-term survivors after allogeneic hematopoietic cell transplantation—a single-center real-life cross-sectional study. Front Med. 2022;9.

36. Abu-Tineh M, Ali EA, Alshurafa A, Nashwan AJ, Albsheer K, Ahmed A, et al. The Impact of Tyrosine Kinase Inhibitors on Fatherhood in Patients With Chronic Myeloid Leukemia: A Mixed-Method Study. Cureus. 2023;15(1):1–7.

37. Wei K-C, Sy C, Wu S-Y, Chuang T-J, Huang W-C, Lai P-C. Pneumocystis jirovecii pneumonia in HIV-uninfected, rituximab treated non-Hodgkin lymphoma patients. Sci Rep. 2018;8(1):8321.

38. Lanzhu L, Jinhua H, Ziyao X, Ming H, Qian S, Sixuan Q, et al. 伴低T3 综合征的急性髓系白血病 患者的临床特征和预后分析. 2021;42(11):923–9.

39. Lebbink CA, van den Bos C, Dierselhuis MP, Fiocco M, Verrijn Stuart AA, Lentjes EGWM, et al. Thyroid Profile in the First Three Months after Starting Treatment in Children with Newly Diagnosed Cancer. Cancers (Basel). 2023;15(5):1–11.

40. Sciacchitano S, De Vitis C, D'Ascanio M, Giovagnoli S, De Dominicis C, Laghi A, et al. Gene signature and immune cell profiling by high-dimensional, single-cell analysis in COVID-19 patients, presenting Low T3 syndrome and coexistent hematological malignancies. J Transl Med [Internet]. 2021;19(1):1–19. Available from: https://doi.org/10.1186/s12967-021-02805-6

41. Gao R, Chen RZ, Xia Y, Liang JH, Wang L, Zhu HY, et al. Low T3 syndrome as a predictor of poor prognosis in chronic lymphocytic leukemia. Int J Cancer. 2018;143(3):466–77.

42. El-Kareem SAA, Ebied SAEM, Sadek NA, Saad DM, Nadwan EA. Serum estrogen and its soluble receptor levels in Egyptian patients with acute leukemia: case-control study. Egypt J Med Hum Genet. 2021;22(1).

43. Erlandsson MC, Ohlsson C, Gustafsson JÅ, Carlsten H. Role of oestrogen receptors α and β in immune organ development and in

oestrogen-mediated effects on thymus. Immunology. 2001;103(1):17–25.

44. Howell S, Shalet S. Gonadal damage from chemotherapy and radiotherapy. Endocrinol Metab Clin North Am. 1998;27(4):927–43

اطار الدراسة:

استخدمت هذه الدراسة تصميم الحالات والشواهد وركزت على المرضى الذين تم تشخيصهم بسرطان الدم (سرطان الدم الحاد والمزمن على وجه التحديد) والذين تم علاجهم في قسم مدينة الطب/مركز أمراض الدم في بغداد، العراق. تم جمع المعلومات المتعلقة بأعمار الأفراد وجنسهم وملامحهم الجينية ومؤشرات كتلة الجسم، من فبراير 2022 إلى أكتوبر 2022.

الهدف من الدراسة:

كان هدف هذه الدراسة هو التحقيق في تأثير التغيرات في الهرمونات التناسلية على الاستجابة المناعية للأفراد الذين تم تشخيص إصابتهم بسرطان الدم.

الملخص

الخلفية: ترتبط اللوكيميا بالتغيرات المناعية والغدد الصماء. وقد أثبتت العديد من الدراسات وجود علاقة بين اختلال التوازن في هرمونات الغدة النخامية والستيرويدات الجنسية وبدء المرض في أحد الجنسين أو كليهما. وكان هدف هذه الدراسة هو التحقيق في تأثير التغيرات في الهرمونات التناسلية على الاستجابة المناعية للأفراد الذين تم تشخيص إصابتهم باللوكيميا.

الطرق: تم تسجيل ما مجموعه 130 مريضًا في الدراسة، بما في ذلك 80 مريضًا تم تشخيص إصابتهم باللوكيميا، و45 مريضًا تم تشخيص إصابتهم باللوكيميا النقوية الحادة(AML) ، و35 مريضًا تم تشخيص إصابتهم باللوكيميا الليمفاوية الحادة .(ALL) وشملت الدراسة 50 من الضوابط الأصحاء. تم قياس مستويات استراديول(E2) ، وثلاثي يودوثيرونين(T3) ، والهرمون المنبه للجريب(FSH) ، والبروجسترون باستخدام كل من ELISA وطريقة اختبار المناعة الفلورية.

النتائج: أظهرت نتائج الدراسة ارتفاعًا كبيرًا في مستويات البروتين التفاعلي سي (CRP) والفيريتين ونسبة العدلات إلى الخلايا الليمفاوية (NLR) في مجموعة المرضى مقارنة بمجموعة التحكم. ارتفع مستوى البروجسترون في المصل لدى المرضى الذين تم تشخيصهم بسرطان الدم النخاعي الحاد وسرطان الدم الليمفاوي الحاد مقارنةً بمجموعة التحكم. ارتفع مستوى هرمون FSH في سرطان الدم النخاعي الحاد وانخفض في سرطان الدم الليمفاوي الحاد. وقد وجد أن هذا الاختلاف ذو دلالة إحصائية. كما وجد أن مستويات هرموني E2و T3انخفضت بشكل كبير لدى كل من مرضى سرطان الدم النخاعي الحاد وسرطان الدم الليمفاوي الحاد مقارنةً بمجموعة التحكم.

الخلاصة: تقدم نتائج الدراسة دعمًا تجريبيًا لتأثير الهرمونات على الاستجابة المناعية في تطور سرطان الدم.

الكلمات المفتاحية: سرطان الدم النخاعي الحاد (AML)، سرطان الدم الليمفاوي الحاد (ALL)، استراديول، الاستجابة المناعية، وثلاثي يودوثيرونين (T3).

وزارة التخطيط
الجهاز المركزي للتقييس والسيطرة النوعية
مديرية براءات الاختراع والنماذج الصناعية

تأثير تغيرات الهرمونات التناسلية على الاستجابة المناعية لدى مرضى اللوكيميا بما فيهم العاملين في المختبرات الكيميائية

الدكتورة جنان عزيز ثابت

2024