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The Impact of Some Biochemical Factors in Increasing Disease Pathogenicity of Systemic Lupus Erythematosus

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Abstract:

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease with unknown etiology, though genetic and environmental factors appear to play a role in its pathogenesis. In particular, infectious processes are linked to the onset and exacerbation of SLE. The aim of the current study was to understand the relationship between some biochemical factors in SLE patients. 105 blood samples from both genders were collected. ELISA technique was used for detecting specific procalcitonin, vitamin D and calcium. The results of this study showed that SLE patients recorded the lowest percentages of calcium (7.36 ± 0.10 mg/dl) than control (11.97 ± 2.12 mg/dl), and vitamin D (7.79 ± 0.58 pg/ml) than control (22.10 ± 4.83 *pg/mL*). And the highest percentage of procalcitonin level in serum (35.73 ± 4.08 pg/ml) compared to the control (11.57 ± 5.35 pg/ml). Furthermore, the seroprevalence of SLE patients was the highest in the 31-45 years age group, and the majority of them were females which accounted 87.5 %. In this study vitamin D and calcium were the lowest in SLE patients. The severity of disease symptoms in SLE patients may be caused by specific alterations in vitamin D and calcium homeostasis. And procalcitonin was the highest in SLE patents.

Keywords: Systemic lupus erythematosus, Procalcitonin, Vitamin D, and Calcium

تأثير بعض العوامل الكيموحيوية في زيادة الامراضية في داء الذئبة الحمراء

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الخالصة:

داء الذئبة الحمراء هو مرض التهابي مزمن ضمن المناعة الذاتية نتيجه مسببات غير معروفة، على الرغم من أن العوامل الوراثية والبيئية يبدو أنها تلعب دورًا في إحداثه. على وجه الخصوص، ترتبط العمليات المعدية ببداية وتفاقم مرض الذئبة الحمراء. تهدف هذه الدراسة لفهم العلاقة بين بعض العوامل الكيموحيوية في مرضى الذئبة الحمراء. شملت هذه الدراسة 105 عينة من مرضى داء الذئبه الحمراء لكلا الجنسين. أستخدامت تقنية الامتزاز المناعي المرتبط بالانظيم لقياس بروكالسيتونين، فيتامين د، والكالسيوم. أظهرت نتائج هذه الدراسة اقل نسبة للفيتامين د في مجموعة المرضى (7.79±0.58بغ/ملم) بالمقارنه مع مجموعه الاصحاء(22.10 ± 4.83بغ/ملم) والكالسيوم (7.36±0.10مغ/دسل) في مجموعة المرضى بالمقارنة مع مجموعه الاصحاء (11.97 ± 2.12مغ/دسل). وكانت اعلى نسبة للبروكالسيتونين في مصل المرضى (35.73±4.08بغ/ملم)

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بالمقارنة مع مجموعة الاصحاء (5.35 ± 11.57بغ/ملم). علاوة على ذلك، كان معدل الانتشار لمرضى الذئبة الحمراء هو الاعلى في الفئة العمرية (31.–45), وغالبيتهم من الإناث بنسبة 87.5٪. في هذه الدراسة ، وجد ان فيتامين (د) والكالسيوم يكونان في أدنى مستوياتهما في مرضى الذئبه الحمراء. قد تكون شده المرض في مرضى الذئبه الاحمراري ناجمة عن تغيرات معينة في فيتامين د وتوازن الكالسيوم. وكان تركيز البروكالسيتونين هو الأعلى في مصل مرضى الذئبه الحمراء.

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Introduction

Systemic lupus erythematosus **(**SLE) is an immune disorder that primarily affects women of reproductive age. In this disease, multiple autoantibodies are detected in the blood, each of which binds to a different nuclear antigen, such as double-stranded DNA, Smith (Sm) and ribonucleoproteins (RNP). These autoantibodies cause inflammation in a variety of organs, including the skin, kidneys and joints [1]. SLE origin is yet unknown. However, a major genetic contribution to illness development is suspected. Single nucleotide polymorphisms (SNPs), gene shortages and duplications, and abnormal splice variant expression have all been linked to its development in some people [2]. There are some biochemical factors concerned in increasing disease pathogenicity in SLE patients. Calcium (Ca) is important in both cellular compartments. Its signals are undeniably important in B cell growth and destiny, both of which are important features of immunological tolerance. Furthermore, according to recent studies, the cyclic guanosine monophosphate adenosine monophosphate (GMP-AMP) stimulator / synthase of antiviral medication genes axis is activated by a metal signal; therefore assisting resistance regulation via type I interferons [3][4]. There is still more research to be done on the clinical importance of serum calcium levels in SLE patients. Ca responses in SLE cells expand after the antigen receptor interest, according to concentrations. T cells from SLE patients with committed T cell receptors produce more inositol 1,4,5-triphosphate (IP3) and receive more calcium from the endoplasmic reticulum [5]. The effects of IP3 on diastolic (Ca2+) and Ca2+ transient amplitude is most strong in the nuclear area. Atrial myocytes are more sensitive to IP3 uncaging than ventricular cells at shorter laser exposure durations, and the overall effects on cytosolic, nuclear and subsarcolemmal Ca2+ transient amplitudes is greater after IP3 uncaging [6].

There is a relationship between Ca and vitamin D (Vt D) [7]. Vt D is a steroid hormone that is essential for Ca metabolism and bone health [8]. Vt D has been shown to have an important role in a variety of systems, including the immune system, muscles, cancer, cellular development and differentiation, and the vasculature [9]. T cells, B cells, and dendritic cells are all impacted negatively by Vt D regulatory role in immune response modulation [10]. Because of its immunologic suppressive properties, it has been speculated that it may play a role in autoimmune disorders like SLE [9]. In persons with lupus, antiphospholipid antibody-induced thrombosis risk increased disease activity and tiredness have all been linked to Vt D insufficiency [11]. Importantly, Vt D administration has been associated with reduced proteinuria, increased complement levels and improved overall disease activity in SLE, according to both an observational cohort and randomized controlled research [12].

Procalcitonin, the peptide procalcitonin (PCT), is a precursor to the hypocalcemic calcitonin hormone and has been used as a systemic infection marker. It has 116 amino acids and has been fully understood since 1984 [13]. PCT is a hormone-free glycoprotein that is the propertied of CT. There are 116 amino acids in it with 13 KD molecular weight [14]. It is normally produced by the thyroid glands C-cells. Then a particular protease breaks down PCT to produce CT, katacalcin and an N-terminal residue [15]. The quantity of PCT in the blood has been found to be an effective diagnostic for identifying and monitoring bacterial and

fungal infections in the body [16]. It is not raised in healthy individuals; however, it is somewhat elevated in viral or localized bacterial infections [17]. Infection is more common in patients with SLE [18].

Materials and Methods

One hundred and five (105) blood samples from SLE patients and controls of both genders (72 females and 33 males) with ages ranging between 15 to 60 years, were taken between October 2020 and February 2021. The blood samples were collected at Al-Elwiya Educational Hospital and from out clinics. Prior to the collection of blood samples from each participant under study, an information sheet was created and designed using a questionnaire that covered a variety of information. Five milliliters of blood was drawn from each participant's redial vein using disposable syringes. Every single sample of blood was put into a gel and clot activator tube. They were then separated into three Eppendorf tubes using micropipettes and centrifuged at 3000 rpm for 10 minutes before being stored at -20ºC until the biochemical variables were measured.

Serology

Enzyme linked Immunosorbent Assay (ELISA) kit (Elabscience, USA) was used for detection specific, Procalcitonin ELISA (RDEEH0341), vitamin D ELISA (E-EL-0014) and calcium (E-BC-K103-M) in the sera of all subjects, according to the manufacturer's instructions.

Statistical Analysis

To identify the impact of various factors (Vt D, Ca, and PCT) on studying SLE patients, Statistical Analysis System- SAS (2012) software was employed. In this study, significant comparison of means was performed using the least significant difference (LSD) test [19]. Statistics were considered significant at P values less than 0.05.

Results

Table 1 summarizes the demographic distribution of the study groups by age. The findings showed that patients' ages ranged from 15 to 60 years old, with a mean age of 42.8 ± 2.0. And that the majority of SLE patients (44%) were between the ages of 31 and 45 and control was 52 % between the ages of 15 and 30, while the lowest percentages of SLE patients and control were in the age group of 46 to 60. That variation between researchers' results may occur due to the impact of geographic distribution of all samples , as well as the different ways in which patients responded to infection due to their individual immune system [20].

Table 1: The distribution of percentages of SLE and control based on ages.

Age (years)	SLE%	Control%	P value
15-30	12 (24 %)	26 (52 %)	0.05
31-45	22 (44 %)	14 (28 %)	0.05
46-60	16 (32 %)	10 (20 %)	0.05

Highly significant different ($P < 0.05$)

The gender distribution of the analyzed groups revealed that the majority of SLE patients were females with a higher ratio than males 49 (87.5 %) (Table 2). The higher prevalence of SLE in females may be due to the differences in the metabolism of sex hormones and/or gonadotropin releasing hormone (GnRH) [21]. The results suggested that hormonal variations

and their impact on the immune response may be the cause of the higher incidence of SLE in females than in males [22]. Women produce more helper T cells as a result of these variables, and since these cells operate as stimulators, they may assist autoimmunity development [21].

Table 2: The distribution of percentages of SLE and control based on gender.

Gender	SLE%	Control%	P value
Female	49 (87.5 %)	23 (46 %)	0.05
Male	6 (12.5 %)	27 (54 %)	0.05

Highly significant different ($P < 0.05$)

The typical level of calcium in a healthy person's serum is 9-13 mg/dl. This study showed highly significant difference ($P < 0.05$) between SLE patients and the control. In SLE patients' sera (7.36 ± 0.10 mg/dl), as shown in Table 3, was lower than the control (11.97 ± 2.12 mg/dl). Calcium levels may be more important in the SLE disease process than previously thought. Hypocalcemic events are more common in SLE patients [23]. As a result, changes in total serum calcium levels in our study SLE patients could have contributed to the drop in serum albumin level [23]. Albumin levels in renal disease are indirect indicators of renal loss due to proteinuria. Albumin is also used to assess protein and energy/nutritional status. Kidney injuries in patients with SLE patients reduce the albumin level, thus reducing calcium [24]. More research should be conducted to investigate the changes in various calcium types in SLE patients and to uncover the underlying mechanisms by which SLE disease activity impacts the body calcium homeostasis [23].

Table 3: Procalcitonin, calcium and vitamin D levels in SLE patients and healthy control group.

Parameters	SLE	Control	P value	LSD value
Calcium	Mean ± SE 7.36 ± 0.10 mg/dl	Mean ± SE 11.97 ± 2.12 mg/dl	0.05	1.836
Vitamin D	7.79 ± 0.58 pg/mL	22.10 ± 4.83 pg/mL	0.05	6.473
Procalcitonin	35.73 ± 4.08 pg/mL	11.57 ± 5.35 pg/mL	0.05	11.415

Highly significant different ($P < 0.05$)

In the SLE patients in the current study (Table 3), there was a highly significant difference ($P \leq 0.05$) between SLE patients (7.79 ± 0.58 pg/mL) and the control (22.10 ± 4.83 pg/mL). Low concentrations vitamin D levels are linked to disease activity and to osteoporosis, weariness and depression [25]. SLE patients have certain cardiovascular risk factors. The relationship between hypocalcemic events was examined [26] with total serum calcium, and vitamin D levels among those with SLE. Due to the use of medications such as glucocorticoids, anticonvulsants, antimalarials and calcineurin inhibitors as well as the avoidance of sunlight, photoprotection, renal insufficiency and other factors, hypovitaminosis D is quite common in SLE. Vitamin D metabolism or vitamin D receptor activities are downregulated [26].

Calcium and vitamin D are inversely correlated, with calcium increasing vitamin D and vice versa. As excessive vitamin D levels in the body cause calcium levels to rise, calcium is represented in the above table in high proportion. [27].

The recent investigation discovered a highly significant difference ($P<0.05$) in PCT levels between SLE patients (35.73 ± 4.08 pg/ml) and the healthy control group (11.57 ± 5.35 pg/ml) (Table 3). In febrile SLE patients, PCT is a biomarker of bacterial infection.

PCT levels rise in acute inflammation in response to bacterial endotoxin and inflammatory cytokines [28]. It was discovered that high PCT can be used to accurately differentiate bacterial infection from an SLE flare and that PCT is a helpful diagnostic biomarker for bacterial infection in SLE patients. However, doctors should be cautious that normal PCT levels do not completely rule out the possibility of a persistent infection. A thorough investigation of infection sources should always be prompted by high PCT levels in SLE patients [29].

Conclusion

This study concluded that SLE patients had lower levels of Ca, Vt D and high PCT levels . In addition, the percentage of females was the largest among patients with SLE.

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