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The diagnostic role of the complement C3, C4 in patients with systemic lupus erythematosus

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Abstract
The aim of this study is to substantiation the impact of C3, C4 in patients with Systemic lupus erythematosus. During the period 2/January/2019 to 1/October/2020, thirty three patients (32femal: 1male) with Systemic lupus erythematosus that diagnosed by specialist with ages ranged between (15-60) years, by using C3, C4 immunturbidimetric test. of all patient, 33% have low level of serum C3, 12% have low level of serum C4.

Keywords: autoimmunity, systemic lupus erythematosus, C3, C4

Introduction

The immune system is a network of molecules, cells, tissues and organs that work together to defend the body against pathogens, but sometimes a failure occurs in the mechanisms of immune recognition, so the immune system becomes unable to distinguish between self and non-self antigens and begins to produce antibodies directed against them. Its antigens attack its own cells and tissues [1] Systemic lupus erythematosus is an autoimmune disease characterized by the production of antibodies to components in the cell nucleus in association with various clinical manifestations [2]. Clinically, lupus erythematosus affects adults, especially women of reproductive age (20-40 years), female infection rate for males It is (1: 10) in favor of females, and lupus erythematosus can affect children, as 8% to 15% of patients are children [3]. Estrogens, in particular, (17-oestradiol) and their metabolites play an important role in lupus erythematosus [4].The primary pathological findings in a patient with lupus erythematosus are inflammation and deposition of immune complexes leading to inflammation at the site of the deposition [5]. The exact pathogenetic mechanism of lupus erythematosus has not been revealed exactly, as lupus is associated with a family history, especially among first-degree relatives, and lupus may be associated with other autoimmune diseases such as autoimmune anemia, immune thrombocytopenic purpura and thyroiditis. Genetics play an important role in increasing the predisposition to the disease, but most cases of lupus erythematosus are single cases without the presence of a genetic factor and this suggests that environmental factors may be responsible for the development of the disease [6].

The complement system consists of a network of regulatory proteins that form an important part of the endothelial immune system. Some of these proteins are soluble in plasma and some are fixed on the surface of cells. The primary function of the complement components is to stop the invasion of microbes. Activation of the complement leads to the denaturation of the pathogen, its removal by phagocytes and the dissolution of its cell wall [7]. Complement activation occurs in three different ways: the classical pathway, the alternative pathway, and the stream of lectin-dependent proteins. Complement proteins are inactivated in the plasma and with the appropriate signal they are sequentially activated in a cascade manner. The three pathways converge at the C3 component (which constitutes the most abundant complement protein in plasma) and as a result of activation, compounds (CC36, C5, C5) are formed, which play an essential role in complement functions. But it includes important regulators and activators of many cellular and humoral immune functions [8].

The association between the complement system and lupus erythematosus is a paradoxical inverse association, where the increased activation of the complement system was associated with an exacerbation in the case of patients [9]. In particular (C3, C4) carry a high risk of disease progression as deficiency of complement compounds leads to inappropriate clearance of necrotic residues and immune complexes, and impaired clearance of immune complexes is a major factor contributing to the pathogenesis of systemic lupus erythematosus [10].

The second theory is based on the important role that complement plays in autoimmunity by determining the threshold for T and B cell activity, where it was shown that there is an important regulatory role for the complement in protecting against the immune response to autoantigens and in promoting lymphocyte killing. self-actualized. [11] During this study, complement levels (C3,C4) were calibrated in a group of lupus erythematosus patients to see if they had a role in diagnosing the disease.

The importance of the research

given the increasing spread of autoimmune diseases and the difficulty of treating this type of disease in case of delay His discovery The search for specific diagnostic factors has become an urgent necessity. Complementary

tests are distinguished from the rest of the laboratory analyzes related to autoimmunity, with ease of procedure and low cost, and this reduces the burden on the patient and the laboratory at the same time.

Research Objectives
To measure the serum levels of complement proteins C4 and C3 in a group of patients with lupus erythematosus who are in the process of diagnosis.

Methods and Materials
The group of patients included (33) patients diagnosed with lupus erythematosus, their ages ranged between (15-60) with an average age of (29) years. and blood samples were collected from the patients before they underwent any treatment.

Serum collection: The consent of the patients was taken before taking the sample, and then the blood was collected in a dry, emptied tube, and then the sample was left to coagulate at room temperature for half an hour, and then the blood samples were collected. The tube was turned on and then we isolated the serum and stored it at a temperature of (-20) Celsius until all samples were collected.

Laboratory tests: C3, C4 levels were determined using a kit for the British company Biorex using the principle of Immuno turbidometry.

Biostatistics analysis
Statistical analysis was done using the spss program. The normality of the distribution of samples was selected using the Kolmogrove Smirnove test, Mann-Whitney test for comparison of parametric variables and chi-square test to study the association between landmarks and differences.

The results
The study included 33 patients with lupus erythematosus(32 females and males) and 30 persons as a control group, the mean age of patients was (29 years) and the average age of the control (31 years). Out of (33) patients with lupus erythematosus, (11) patients had C3 levels lower than normal values, and there were (22) patients whose C3 levels were normal, and the control sample was all normal. As for the C4 test, there were (4) patients with low levels, and all values were normal in the control group. Antinuclear antibody (ANA) test was positive in (31) patients The test was negative in two patients out of (33) patients. As for the control sample, there was one positive result and the rest of the samples were negative. These results were summarized in the following table:

Table 1

Test		SLE	Control
C3	normal	22	30
	decrease	11	0
C4	normal	29	30
	decrease	4	0
ANA	Negative	2	29
	positive	31	1

Discussion
Lupus erythematosus is an autoimmune disease of unknown pathogenesis. It is a complex mixture of clinical manifestations. SLE has been defined as a group of diverse disorders and clinical manifestations that range from life-threatening diseases. Directly by affecting basic organs such as the heart, lung and kidney. The complement system has an important function as an immune component, but abnormal activation can lead to tissue damage, and complement deficiency leads to infection and also the development of autoimmune diseases, especially lupus erythematosus. [12] There are three main ways to activate the complement: the classical, alternative, and lectin pathways. Regardless of the activated pathway, complement activation is the formation of some components that stimulate macrophages and other immune cells, and the formation of the membrane-attacking complex that dissolves invading cells. Complement is a double-edged sword: proper activation is necessary in order to kill bacteria and remove cooperating residues, while excess activation can cause tissue damage and exacerbate tissue injury, but this theory remains controversial [9].
In the current study, C3 and C4 levels were measured in the serum of patients with lupus erythematosus. C4 was chosen as a component of the classical pathway or lectin, as it is the easiest to titrate among all the components, in addition to the C3 component, which is the main component of the complement and the most abundant in serum. In addition, measuring them together can improve our understanding of the pathological mechanisms of lupus erythematosus that the complement may be involved in in this study. 33% of patients had low levels of C3, and the rest of the patients had normal levels. When compared with the control group, there were statistically significant differences between the two groups, in terms of the C4 component, there was a decrease in the value

of C4 in (12%) of patients. In comparison with the control group, there were no statistically significant differences between the two groups.

These results can be explained by the presence of increased activation of the classical pathway and consumption of components with a decrease in production and an increase in demolition. This decrease can also be attributed to the presence of homozygous or heterozygous deficiency in the production alleles (C3, c4), where the researcher Einav and his colleagues found in 2002 The development of lupus erythematosus in the absence of overactivation of the classical complement pathway and the variant suggests an absence of C3 and C4 production alleles and has been considered as a criterion in the pathogenesis of SLE [13].

In 1973, a study was conducted on 55 patients with lupus erythematosus and it was found that low levels of C4 are the most common among the group of patients.

One of the hypotheses that has been proposed for the emergence of autoimmune diseases in those seeking complement components is a disturbance in the removal of cellular debris and precipitated immune complexes. It induces autoimmune diseases. The capture of autoantigens by dendritic cells and the subsequent induction of T cells and the production of self-active B cells and autoantibodies, as well as a decrease in the rate of immune complexes deposited, leads to local inflammation and damage, as the complement system plays a major role in the removal and cleaning of immune equipment and cellular debris. For the dying cells, especially the components of the classic C1, C2, and C4 pathways that are essential in this process [14].

Another theory is a defect in self-tolerance, which may occur in people who return to complement components. Studies conducted in mice confirmed that during the maturation of the complement immune system, it plays a role in eliminating self-reactive lymphocyte in dendritic follicular cells of peripheral lymphoid tissues. Like the spleen and lymph nodes, CD35 (CRI) and CD21 (CR2) receptors help to recognize autoreactive B cells by binding and presenting autoantibodies to these B cells, and the complement system acts as a link between natural and acquired immunity [14].

In addition to the emergence of some evidence for the involvement of the complement in the pathogenesis of some autoimmune diseases such as systemic lupus erythematosus, as there is sufficient histological evidence that the complement causes tissue damage in SLE, fluorescent studies have demonstrated the deposition of immunoglobulins and complement in the glomeruli and in the walls of the kidneys. Skin vasculature and deposition of immune complexes in the kidney mediate the over-activation of complement and deposition of complement components. Some patients also showed low levels of CRI, which mediates the clearance of circulating immune complexes [14].

Conclusions

The results of the applied study conducted on a group of lupus erythematosus patients indicate that there is an inverse relationship between the presence of the disease and the levels of complement C3, C4, and a decrease in C3 levels was the most common, and the relationship was significant and statistically significant between a decrease in C3 levels. And the presence of disease. The relationship between low levels of C4 and the presence of the disease is not significant, and therefore it is recommended to perform the C3 complement test when the presence of systemic lupus erythematosus is suspected. However, the antinuclear test remains the most sensitive test despite its low specificity.

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