CORRELATION OF C-REACTIVE PROTEIN WITH OTHER SEROLOGICAL MARKERS IN NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Abstract -

Background - Due to disease heterogeneity, low sensitivity and specificity of immunological tests, and other factors make Systemic lupus erythematosus (SLE) diagnosis difficult and then monitoring their disease activity .The C-reactive protein (CRP) rises rapidly in response to inflammation and some autoimmune diseases. The role of CRP in SLE remains controversial. However, CRP enhances the clearance of apoptotic cellsthat likely contributes to homeostasis to SLE.

Aim of study - This study aimed to investigate serum CRP level in newly diagnosed SLE patients and correlate it with certain immunological tests such as Antinuclear Antibodies (ANA), double-stranded DNA (dsDNA), complements C3, C4. And with Erythro Sedimentation Rate (ESR).

Patients and Methods - Eighty-eight patients with SLE according to the classification criteria of the European League Against Rheumatism / American College of Rheumatology (EULAR / ACR) and 70 healthy controls were collected in this study. Sample were subjected to immunological and biochemical tests.

Results - The results show that CRP, ESR, ANA, dsDNA, C3 and C4 showed a significant higher in SLE patients than in healthy controls. However CRP still in SLE patients within the normal range.We found a significant correlation between CRP with dsDNA, whereas no correlation was detected with other parameters.

Conclusion - The CRP is a non-specific marker for lupus disorders but is associated with the dsDNA.

Keywords - Systemic Lupus erythematosus, ESR, ANA, C-Reactive protein, C3, C4

I. INTRODUCTION

Systemic lupus erythematosus(SLE), is a an autoimmune disease characterized by abnormal production of a wide and heterogeneous range of autoantibodies[1]. It'll mainly affect females in puberty and menopause. The incidence ratio of female/male is 9/1[2]. The complicity of this disease appeared in its effect on clinical features such as renal, neurological disorders or inducing arthritis [3]. It is also associated with an increased risk of premature death [4].

In patients with SLE, distinguishing between infection and disease activity might be difficult, doing so will benefit in medication decisions. With increasingly sensitive means of testing for CRP, CRP may help distinguish infection from active disease in patients with SLE.[5]C-reactive proteinserum level is frequently related with the level of IL6 and is routinely assessed as a marker of inflammation in a range of disorders. However, despite elevated IL6, CRP often decreases in autoimmune illnesses (SLE)[6]. The CRP levels affected by many parameters such as age, body mass index (BMI), infection, medications, cardiovascular accidents and malignancy [7] and[8]. The ability of CRP to accelerate the clearance of apoptotic cells as well as its tendency to bind to nuclear antigens led to the idea that CRP could prevent autoimmunity by masking or promoting self-antigens from the immune system[9].

Generally, In SLE especially in its systemic form, autoantibodies directed to nuclear (ANAs), cytoplasmtic, and cellular membrane antigens are considered the serological hallmark. [10].

Complement activation showed pivotal role in pathogenesis of SLE- associated immune complex damage. In addition to its function in fighting infectious diseases, it also plays a key role in the inflammatory response induced by immune complex deposition especially in SLE[11].

Complement dysregulation, mainly in C3 and C4,is well documented during the course of the SLE. As a result, it is used as a biomarker for SLE monitoring[12].

However, inherited deficiencies in the complement system show an independent predisposition of

affected individuals to bacterial infection and SLE[11].

Moreover, SLE patients had a higher incidence of elevated ESR from CRP comparing with from rheumatoid arthritis patients, although elevated ESR was associated with both lupus activity and infection, making the distinction between lupus and infection unclear. On the other hand, ESR elevations are closely associated with SLE exacerbations[13].

Present work aimed to evaluate the C-reactive protein serum level in newly diagnosed SLE patients and to help distinguishing between flare-ups and infections and to determine the association of CRP and other markers ESR, C3, C4, dsDNA, and ANA. That may facilitate treatment determination and long term disease monitoring.

II. PATIENTS AND METHODS

This is a case-control study conducted in Rheumatology Unit /Baghdad Teaching Hospital, Baghdad medical city, Baghdad, Iraq. Eighty-eight patients were included in this study with new diagnosis of SLE according to the European League Against Rheumatism/ American College of Rheumatology (EULAR /ACR) classification criteria of SLE. Seventy healthy volunteers were included also as a control group. All subjects provided ethical informed consent. This study was approved by the ethical committee of the College of Medicine/Al-Nahrain University International Review Board (I.R.B).

A 5 ml of venous blood were drawn from all subjects using a single-use syringe, 2ml out of them was transferred to the ethylene diaminetetraacetic acid (EDTA) tube for ESR test (AFCOVAC, Spain). A 3 ml out of 5 ml of drawn blood was dispensed into a vacuum tube and left at room temperature for 15 minutes to clot. Finally, it's centrifuged (using Rotofix 32A centrifuge, German) at (13,000 rpm) over 20 minutes. These prepared samples were used to measure the laboratory tests as following : ANA, and dsDNA kit (Aesku, Germany), C3 and C4 (LTA, Italy) and CRP kit (Roche, USA). Statistical analysis was performed using SPSS version 24. An unpaired t-test was used to find the significant difference between the two groups. A person correlation test is used to test the correlation between the CRP and other parameters. The significant p-values were 0.05.

III. RESULTS

It was recorded that most of SLE affected patients are females74 (92.5%) comparing to 6 (7.5%) males, pointing to a highly significant difference between them, p-value 0.00001. (Figure-1).

Age and sex matched control group was included in this study, the female in the control group was 64 (91.5%) and the male was 6 (8.5%).

The mean age of SLE patients was 30.95 ± 8.25 years comparing to 29.97 ± 8.06 in controls. Body mass index (BMI) of SLE patients was 26.80 ± 4.38 comparing to 26.04 ± 4.01 in control group ,no significant difference between the two groups , p-value 0.2558. (Table -1)

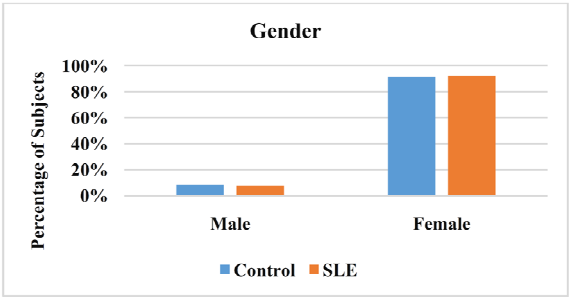


Figure (1): Gender Distribution ofall included subjects.

Characteristics	SLE patients	Control	p-value
Age (years)	30.95 ± 8.25	29.97 ± 8.06	0.4522
Gander			<0.00001*
Female	92.5%	91.5%	
Male	7.5%	8.5%	
BMI	26.80 ± 4.38	26.04 ± 4.01	0.2558

* Significant difference at the 0.05 level.

Table (1): the characteristics of SLE patients and control subjects

BMI: Body mass index.

A highly significant difference were recorded in allstudied parameters (ESR, CRP, ANA, dsDNA, C3 and C4) between patients and controls.Serum levels of ESR, CRP, ANA, and dsDNAfor SLE patients were higher than control. While the C3 and C4 levels were lower in SLE patients than controls (table-2)

Parameters	SLE patients	Controls	p-value
ESR	54.32 ± 3.10	13.42 ±5.34	0.00001*
CRP	2.92 ± 0.47	1.45 ±1.02	0.0006*
ANA	80.36 ± 25.48	2.33±2.29	<0.00001*
dsDNA	29.93 ± 11.62	0.35 ±0.02	0.000023*
C3	45.01 ±28.15	125.92 ±19.17	<0.00001*
C4	11.52 ±2.58	35.57 ±8.05	<0.00001*

* Significant difference at the 0.05 level.

Table (2): Analysis of SLE patient and control subjects' certain parameters (ESR,CRP, ANA, dsDNA, C3 and C4).

ESR, Erythrocyte sedimentation ratio;CRP, C-reactive protein; ANA, Anti-nuclear antibodies;dsDNA, double stranded deoxyribonucleic acid; C3,complement3; C4,complement4

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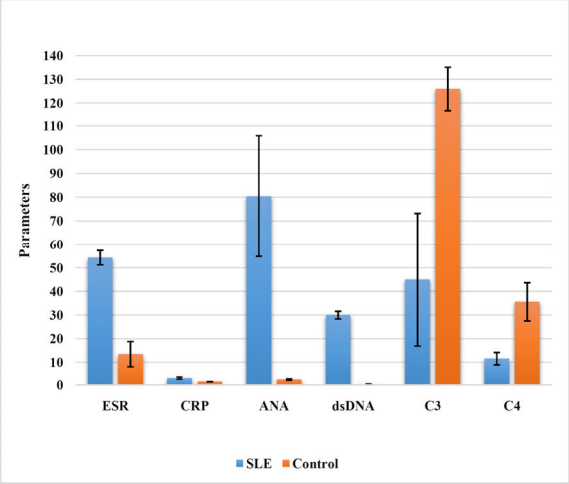


Figure (2): Comparison between SLE patients and Healthy Control Subjects regarding ESR,CRP, ANA, dsDNA, C3 and C4.

A correlation was detected between CRP withdsDNAThose correlationswere recorded as;r = 0.215, p–value = 0.044.

On the other hand, no correlation was detected between CRP and ESR, C3 and C4;rs= 0.088, p–value = 0.414; r = -0.156, p-value= 0.124 andr = -0.150, p–value = 0.162. (Table-3).

Parameter		CRP ( )	
		Patients N=88	Control N=70
ESR (mm/hr)	r	0.088	0.139
	p	0.414	0.250
dsDNA ( )	r	0.215	0.029
	p	0.044*	0.812
ANA ( )	r	-0.187	0.380
	p	0.081	0.001*
C3 ( )	r	-0.165	-0.187
	p	0.124	0.121
C4 ( )	r	-0.150	0.042
	p	0.162	0.732

Table (3): Correlation of CRP withcertain parameters in SLE patients.

ESR, Erythrocyte sedimentation ratio; CRP, C-reactive protein; ANA, Anti-nuclear antibodies; dsDNA, double stranded deoxyribonucleic acid; C3,complement3; C4,complement4

* Significant difference at the 0.05 level.

IV. DISCUSSION

In the present work, it is recorded that most cases are females 92.5% comparing to 7.5% males. The age mean of the studied group is 30.9 years. Those findings come in accordance with other published researches in Iraq and in different nations [2] and [14].

We alsoalsofound that CRP is significantly higher inSLE patients comparing to controsl, however both are in normal range.Several studies have explored that the serum levels of CRP increased as the time of SLE disease increase [15].

We found that in addition to that dsDNAwas significantly higher in lupus patients comparing with controls, a positive correlation was detected between CRP and dsDNA.

In SLE patients,dsDNA and ANA autoantibodies present in advance to the clinical symptoms appearance [16]. The dsDNAantibodies are antibodies released in response to higher-levels serum dsDNA, when an inflammation attacks the body as a response to increasing the immunity of the body. While dsDNA and ANA may be present at a low level with several disorders, it is high primarily associated with lupus. Lupus is strongly associated with a high level of dsDNA in the blood and is often significantly increased during or just before a flare-up. When the dsDNA is positive and the person tested has other clinical signs and symptoms associated with lupus, it means that the person tested likely has lupus. [17].

Normally, antibodies protect against infection and are produced when a person's immune system fails to adequately distinguish between "self" and "non-self." They mistakenly attack the body's healthy cells, causing tissueand organ damage. The dsDNA specifically targets the genetic material (DNA) found in the nucleus of a cell, hence the name "dsDNA." The dsDNA test identifies these autoantibodies in the blood [18].

Kumar Y. and Bhatia A. [19] investigated the role of ANA and led to dsDNA changes in SLE disease. They found that SLE excreted higher levels of ANA than normal people. They destroy the molecular structure and are sometimes categorized as strands of DNA.

In our result, the ANA levels in SLE patients show a higher significant value than the normal subjects. The ANA serum is one of the SLE markers for diagnosis of the diseases and monitoring its progression [20] and [22]. It plays an important role in promoting immunity dysregulation and tissue injury through ingestion with the dead lupus cell results as an immune response. These complexes activate the immune system and cause the production of antibodies and inflammation [23]. There is a strong positive correlation between the CRP values and dsDNAin this study. So, the dsDNA levels varying as a response to CRP variation and vice Versa.

IV. CONCLUSION

In conclusion, The C-reactive protein is a valuable and sensitive marker to predict lupus disorders and is associated with patients dsDNA.

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