Serum Neopterin Level in Systemic Lupus Erythematosus: Relation to Disease Activity, Organ Affection and Different Therapy Regimens

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ABSTRACT

Distinguishing patients with active systemic lupus erythematosus (SLE) from those with inactive disease has always been considered a great challenge. Identifying new sensitive markers of activity will be of great value in the clinical management of the disease. Thus the aim of the current study was to investigate the relationship between serum neopterin levels and various parameters of disease activity currently used, in addition, to investigate serum neopterin levels in different patterns of organ disease involvement and during the administration of different therapy regimens used in the management of SLE. The study was conducted on 75 female subjects; 26 patients with active SLE, 24 SLE patients in remission and 25 healthy controls. Patients with SLE were fulfilled four or more of the American Rheumatism Association (ARA) criteria, and disease activity was scored using the British Isles Lupus Assessment Group (BILAG) index. Erythrocyte sedimentation rate (ESR), serum urea, serum creatinine, liver function tests, plasma complements C3 and C4, C3 degradation products (C3dg), anti-double stranded DNA antibodies (anti-dsDNA) and serum neopterin were measured in all groups. Serum neopterin was significantly elevated in the active group as compared to the remission group. Both groups of SLE showed higher levels of neopterin when compared to the control group. Serum neopterin level showed higher sensitivity than other SLE markers (80%) and second highest specificity after anti-dsDNA antibodies (73%). Also, a highly significant positive correlation was found between serum neopterin levels and each of plasma C3dg, anti-dsDNA antibodies, and ESR. Meanwhile, a highly significant negative correlation was detected between serum neopterin levels and both plasma C3 and C4 levels. As regarding various treatment regimens used in the management of active SLE, the current study demonstrated decrease in serum neopterin levels in patients receiving combined treatment of both prednisolone and cytotoxic drugs than those receiving either treatment alone. A significant difference in serum neopterin levels was observed in patients with multiple organ affection in comparison to those with single organ affection regardless the type of organ affected. The present results suggest that the estimation of serum neopterin levels seems beneficial in the assessment of disease activity and progress in SLE patients as well as the assessment of the efficacy of various treatment regimens being used.

Key words: *Systemic lupus erythematosus, neopterin, complements, anti-ds DNA antibodies.*

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multisystem, usually life-long, potentially fatal autoimmune disease characterized by unpredictable exacerbations and remissions despite therapy[(1)]. SLE has always been associated with numerous abnormalities in the immune system including activation of both the humoral as well as the cellular immunity[(2)].

One of the greatest challenges of SLE is distinguishing patients with active disease from those with inactive disease (patients in remission)[(3)]. Serologic markers play an important role in the assessment of disease activity in SLE. These markers are critical for understanding the pathogenesis of the disease, monitoring the disease progression, following up the efficacy of the treatment and identifying potential clinical benefits from new therapies[(4)].

Humoral immune system activation in SLE can be reflected on ESR, serum or plasma complement concentrations, and formation of anti-dsDNA antibodies. These parameters are currently used as indicators for disease activity. However, some patients may have abnormalities in the results of these tests for considerable period yet show few clinical symptoms or functional deterioration of a major organ, whereas others are markedly symptomatic with minor aberrations in these tests results [(5)].

Meanwhile, other parameters can be used to indicate primary cellular immune system activation reflecting T lymphocyte upregulation. Particular attention had been focused on neopterin, which had been shown to be an early, specific, and sensitive marker of cellular immune system activation in several clinical settings including autoimmune and inflammatory diseases[(6)].

Neopterin is an aromatic pteridine derived from intracellular guanosine triphosphate produced by human monocyte-derived macrophages upon stimulation with the cytokine interferon gamma (INF- γ) released from activated T- lymphcytes[(7)]. Neopterin production may, also, be triggered by other immune activators including other interferons, interleukin-1α (IL-1α), tumor necrosis factor- α (TNF- α) and lipopolysaccharides. Endothelial cells may, also, produce neopterin in vitro and that production is augmented in the presence of INF-γ in combination with TNF-α[(8)]. Increased amounts of neopterin in human body fluids are found in many disorders, including viral infections, autoimmune diseases, neuro-degenerative diseases, allograft rejection, as well as, certain malignant diseases[(9)].

The aim of the current study was to investigate the possible relationship between serum neopterin levels and various parameters of disease activity currently used. In addition, to investigate serum neopterin levels in different patterns of organ disease involvement and during the administration of different therapy regimens used in the management of SLE.

SUBJECTS & METHODS

The current study was conducted on 50 SLE female patients who fulfilled four or more of the 1982 revised American Rheumatism Association (ARA) criteria for the classification of SLE[10], and 25 healthy female as controls. They were classified into three main groups:

Group I [control group]: included 25 healthy normal females with mean age (mean ± SD) of 27.6 ± 8.3 years.

Group II [remission group]: included 24 female patients with SLE with mean age (mean ± SD) of 29.4 ± 6.6 years.

Group III [active group]: included 26 female patients with active SLE disease according to British Isles Lupus Assessment Group (BILAG) index [11]. Their mean age ± SD was 30.5 ± 7.3 years.

SLE activity was scored by using the BILAG index[11], which consists of 86 questions covering eight organ based systems, namely; general, mucocutaneous, nervous, musculoskeletal, cardiovascular, vasculitis, renal, and hematological systems.

Patients were selected from the Outpatient Clinics and Inpatient Wards of Rheumatology and General Medicine Departments in Kasr El-Aini Hospital, Cairo University. All participants gave their informed consent before participation in the study. All subjects were evaluated by complete history taking including history of organ affection and all the medications used, as well as, thorough clinical examination with special stress on various organs affection.

According to BILAG index, proper history taking and physical examination, 9 patients with active SLE had multi-organ affection while 17 patients had single organ affection. Drug history revealed that 10 active SLE patients were treated by prednisolone only, 7 were treated by cytotoxic drugs only, and 9 were treated by combined treatment of both prednisolone and cytotoxic drugs.

For all subjects the following laboratory investigations were done:

Blood picture: including red blood cell, white blood cell, and platelet counts.

Erythrocyte sedimentation rate (ESR): using Westegern method.

Renal function tests: serum urea [12] and creatinine [13].

Liver function tests: aspartate transaminase (AST) [14], alanine transaminase (ALT) [14] and serum bilirubin[15].

Plasma C3, C4, and C3dg: were detected by a double decker immuno-diffusion method [16].

Antinuclear antibody (ANA) and anti-double stranded deoxyribonucleic acid antibody (anti-dsDNA): were assayed by indirect immunofluorescent assay[17].

Serum neopterin: was measured using a solid phase enzyme-linked immunosorbent assay (ELISA) kit supplied by Cellular Comminication Investigations Immunotech, France[18].

Statistical Analysis:

The results were analyzed using SPSS computer software package, version 10.0 (Chicago-IL, USA)[19]. Data were presented as mean ± S.D. Unpaired student t- test was used for analysis of two quantitative data. Differences among the three groups were compared by one-way ANOVA followed by post-hoc test. To study the relationship between the measured

parameters, Pearson's correlation was calculated. The results were considered statistically significant at $p<0.05$. Re-diagnostic value of variables was assessed using Receiver Operating Characteristic (ROC) curves, the specificity and sensitivity for a given cut-off were calculated (cut-off values = mean ± 2 S.D.).

RESULTS

There was a non significant difference in age between active, remission and control groups ($p>0.05$). There was, also, a non significant difference in duration of the disease between active and remission groups ($p>0.05$) (Table 1).

Table 1: Demographic data of SLE and control groups

	Group I (control) n = 25	*Group II (remission) n =24*	*Group III (active) n = 26*	*p-value*
Age (years)	27.6 ± 8.3	29.4 ± 6.6	30.5 ± 7.3	>0.05
Disease Duration (years)		8.4 ± 5.8	11.2 ± 7.68	>0.05

Values are expressed as means ± S.D *P-value is significant if < 0.05**

Hematological and biochemical data were shown in table 2. There was no significant difference between all studied groups as regard serum levels of total bilirubin, AST and ALT ($p>0.05$). Serum levels of urea and creatinine were significantly higher in active group compared to remission group ($p<0.05$ for both levels) and control group ($p<0.01$ for both levels), while no significant difference in their levels between remission and control groups ($p>0.05$ for both levels).

As regard blood count; white blood cell, red blood cell, and platelet counts, all were significantly lower in active group compared to remission group, as well as, to control group ($p<0.05$ for WBC and RBC and $p<0.01$ for platelets) and control group ($p<0.01$ for each), while comparing remission group to control group, as regarding the above counts, no significant differences were found.

As regard ESR levels, they were significantly higher in active SLE patients in comparison to patients in remission and, also, to controls ($p<0.01$ and $p<0.001$ respectively). Also, ESR levels were significantly higher in patients in remission in comparison to controls ($p<0.001$) (table 2).

Table 2: Hematological and biochemical data of SLE patients and control group

	Group I (control) n = 25	*Group II (remission) n =24*	*Group III (active) n = 26*	*p-value*
Total Bilirubin (mg/dl)	0.88 ± 0.2	0.91 ± 0.23	0.92 ± 0.36	>0.05
AST (U/L)	32.1 ±7.8	33.2 ± 9.3	33.6 ± 11.1	>0.05
ALT (U/L)	30.1 ± 7.6	29.8 ± 8.2	30.4 ± 6.8	>0.05
Urea (mg/dl)	28.8 ± 6.3	31.1 ± 9.7	48.9 ± 20.1 $^{+\#}$	<0.01*
Creatinine (mg/dl)	0.80 ± 0.32	0.88 ± 0.28	1.89 ± 0.84 $^{+\#}$	<0.01*
WBCs (x 10^3/mm^3)	4.0 ± 0.68	3.8 ± 0.7	2.8 ± 0.69 $^{+\#}$	< 0.05*
Platelets (x 10^3/mm^3)	260.2 ± 90.1	248.8 ± 106.3	184.5 ± 95.0 $^{+\#}$	< 0.05*
RBCs (x 10^6/mm^3)	4.5 ± 1.0	4.2 ± 1.3	3.4 ± 1.2 $^{+\#}$	< 0.05*
ESR (mm/hr)	11.1 ± 4.9	45.2 ± 11.5 $^{+}$	78.2 ±21.8 $^{+\#}$	<0.01*

Values are expressed as means ± S.D *p-value is significant if < 0.05**
AST: aspartate transaminase, ALT: alanine transaminase, WBCs: white blood cells, RBCs: red blood cells, ESR: Erythrocyte sedimentation rate.
+: significant p as compared to group I *#: significant p as compared to group II*

Plasma levels of C3 and C4 were significantly lower in active group compared to remission and control groups ($p<0.01$ and $p<0.001$ for both levels respectively), while patients in remission had significant lower plasma C3 and C4 levels compared to controls ($p<0.001$ for both levels) (table 3).

As regarding C3dg levels, they were significantly higher comparing active SLE patients to patients in remission and to controls ($p<0.01$ and $p<0.001$ respectively), also, they were significantly higher comparing patients in remission to controls ($p<0.001$) (table 3).

Anti-dsDNA levels were significantly higher comparing active SLE patients to patients in remission ($p<0.001$), but they were not detected in controls (table 3).

Serum neopterin levels showed a highly significant increase in active group compared to remission ($p<0.001$) and control groups ($p<0.001$), and a highly significant increase comparing remission group to control group ($p<0.001$) (table3) (figure 1).

Table 3: Plasma mean levels of C3, C4, C3dg, anti-ds DNA, and neopterin in SLE patients and control group

	Group I (control) n = 25	*Group II (remission) n =24*	*Group III (active) n = 26*	*p-value*
C3 (mg/dl)	107.4 ± 35.9	78.7 ± 20.6 $^{+}$	62.2 ± 21.9 $^{+\#}$	<0.01*
C4 (mg/dl)	29.3 ± 11.8	17.9 ± 5.9 $^{+}$	10.7 ± 4.7 $^{+\#}$	<0.01*
C3dg (U/ml)	8.1 ± 1.6	12.9 ± 2.5 $^{+}$	14.6 ± 2.7 $^{+\#}$	<0.01*
Anti-dsDNA (IU/ml)	----------	21.2 ± 4.6	39.5 ± 7.7 $^{\#}$	<0.001*
Neopterin (nmol/L)	6.9 ± 1.8	11.6 ± 2.9 $^{+}$	14.5 ± 3.3 $^{+\#}$	<0.001*

Values are expressed as means ± S.D *p-value is significant if < 0.05**
C3: complement 3, C4: complement 4, C3dg: complement 3 degradation products, Anti-dsDNA: anti-double stranded DNA antibodies.
+: significant p as compared to group I *#: significant p as compared to group II*

Active SLE patients receiving combined treatment of cytotoxic drugs and prednisolone showed significantly lower values of serum neopterin compared to those receiving cytotoxic drugs only ($p<0.05$) and to those receiving prednisolone only ($p<0.05$), while comparing those receiving cytotoxic drugs only to those receiving prednisolone only the neopterin serum levels were statistically not significant (table 4) (figure 2).

Table 4: Mean values of serum neopterin levels in the active SLE patients receiving various treatment regimens

	Prednisolone Only n=10	*Cytotoxic Drugs only n=7*	*Combined Treatment n=9*	*p-value*
Neopterin (nmol/L)	15.9 ± 3.9	15.2 ± 3.6	12.4 ± 2.4 $^{+\#}$	<0.05*

Values are expressed as means ± S.D *p-value is significant if < 0.05**
+: significant p as compared to patients receiving prednisolone only
#: significant p as compared to patients receiving cytotoxic drugs only

Serum neopterin levels for patients with SLE activity and multiple organ system affection (n=9) were found to be significantly higher compared to those with single organ system affection (n=17) ($p<0.01$) regardless the specific organ system affected (table 5) (figure 3).

Table 5: Mean values of serum neopterin levels in the active SLE patients in relation to organ affection

	Multiple Organ Affection (n = 9)	*Single Organ Affection (n = 17)*	*P value*
Neopterin (nmol/L)	16.5 ± 3.8	13.4 ± 3.0	<0.01*

Values are expressed as means ± S.D *p-value is significant if < 0.05**

Table 6: Sensitivity and Specificity of ESR, C3, C4, C3dg, anti-dsDNA, and neopterin

	Sensitivity (%)	*Specificity (%)*
ESR	51	47
C3	62	50
C4	70	55
C3dg	65	57
Anti-dsDNA	70	80
Neopterin	80	73

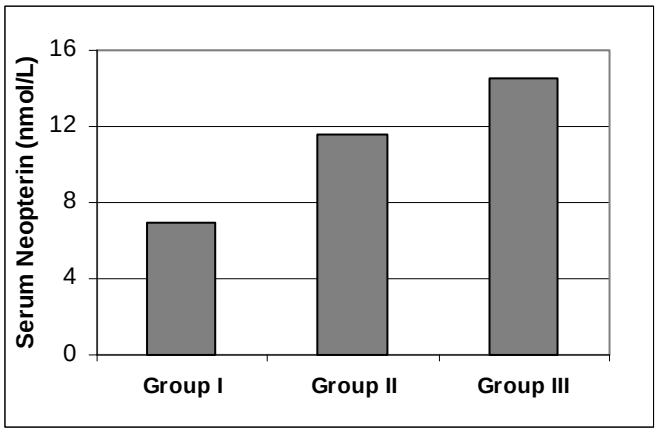

Figure 1: Serum neopterin mean values in SLE patients and control group

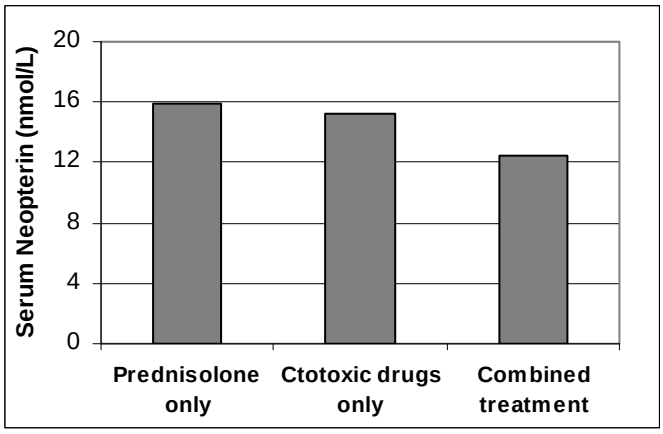

Figure 2: Serum neopterin mean values in the active SLE patients receiving various treatment regimens

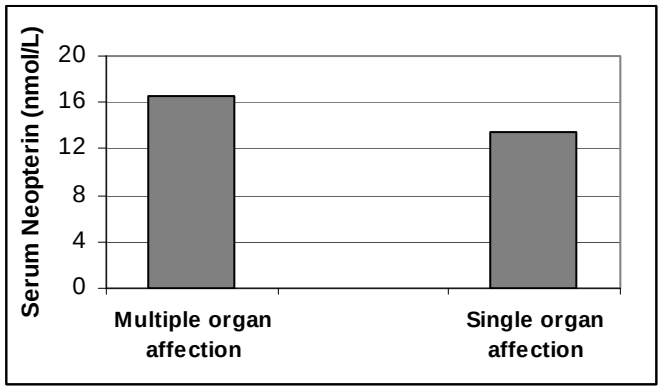

Figure 3: Serum neopterin mean values in the active SLE patients in relation to organ affection

Correlations among the various parameters measured in the current study showed a highly significant positive correlation between serum neopterin level and the following parameters; C3dg ($r = 0.716$, $p<0.001$), anti-dsDNA ($r = 0.71$, $p<0.001$) (figure 4), and ESR ($r=0.699$, $p<0.001$). A significant negative correlation was, also, detected between serum neopterin level and both C3 ($r = - 0.472$, $p<0.01$) and C4 ($r = - 0.680$, $p<0.001$) (figure 5).

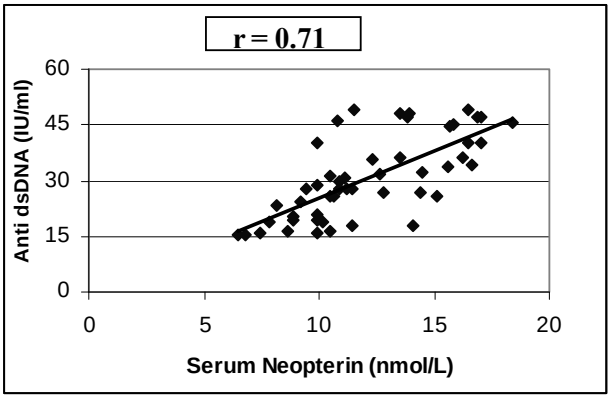

Figure 4: Correlation between serum neopterin and anti-dsDNA (r= 0.71, p<0.001)

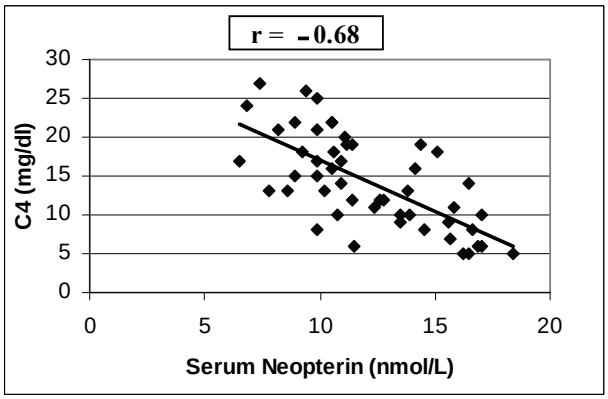

Figure 5: Correlation between serum neopterin and C4 (r= -0.68, p<0.001)

DISCUSSION

Although the many years of study of the disease, the pathology or disease process in systemic lupus erythematosus remains unclear[20].Various laboratory tests were used for detection of the activity of the disease as ESR, plasma complements concentrations, and formation of autoantibodies[21]. Particular attention has recently been focused on neopterin as an important indicator for assessing SLE activity[22,23].

The present study showed significant decrease in RBC, WBC and platelet counts in patients with active SLE compared to patients in remission, as well as, to the healthy controls. Decreased RBC count could be explained by impaired renal function with decreased erythropoietin formation, also due to poor general condition, cachexia and anorexia, in

addition to bone marrow suppression by aggressive cytotoxic therapy [24]. Leucopenia in SLE patients occurs as part of drug toxicity-induced medullar hypoplasia. Also, it may be due to disease activity, bone marrow failure, peripheral destruction and sepsis[25]. The most common mechanism of thrombocytopenia in SLE patients is believed to be increased platelet clearance mediated by anti-platelet auto-antibodies[26].

ESR was significantly higher comparing active SLE patients to patients in remission and healthy controls, and was significantly higher comparing patients in remission to controls.

Plasma levels of C3 and C4 were significantly decreased comparing SLE patients to healthy normal subjects, also, significant decrease in their levels were found comparing active SLE patients with patients in remission. This could be attributed to reduction of their synthesis and, also, their consumption in immune complex formation. These results indicated that complement dysfunction may be an important factor in the pathophysiology of SLE [27, 28]. These results are concomitant with the previous results of Wais et al.[29] who found that people with SLE often have increased ESR and decreased complement levels, especially during the flares of the disease. Arason et al.[30] reported that a functional deficiency of complement had been implicated but not conclusively demonstrated in the pathogenesis of SLE. Nived et al.[31] also, concluded that low levels of components within the classical pathway of complement (especially C3 and C4) have a high specificity for SLE diagnosis.

As regarding C3dg level, the present study showed a significant increase with the same pattern of ESR. This was agreed with Kristina et al., [32] who reported a significant increase in C3dg level in patients with active and inactive SLE compared to normal subjects.

Autoantibodies, particularly antibodies directed against double stranded (ds) DNA are thought to play a role in disease development and progression[33]. The current work demonstrated a significant increase in anti-dsDNA antibodies levels in active SLE patients in comparison to patients in remission. Riemekasten and Hahn [34] reported that high-affinity antibodies to dsDNA are characteristic hallmarks of human systemic lupus erythematosus, and anti-dsDNA antibodies are detected in 30–60% of the SLE sera. Anti-dsDNA and anti-Sm antibodies are highly specific for idiopathic SLE. Gupta and Lim, [35] stated that a combination of anti-dsDNA, serum complement C3 and C4, ESR and CRP, supported by relevant tissue histology, probably provides the most useful information on disease activity, particularly in patients with lupus nephritis. However, results of any laboratory test should always be interpreted with reference to the clinical presentation.

Deocharan et al.[36] reported that anti-dsDNA antibodies are the most frequently detected antibodies in systemic lupus erythematosus. Rising and high titers of dsDNA antibodies suggested an increased risk of progressive disease. Anti-dsDNA antibodies are considered responsible

for much of the kidney disease and renal manifestations that can occur in SLE. However, Isenberg et al.[33] reported that doubts have been raised about their significance and the extent to which they are genuinely part of the pathogenesis of the disease rather than being mere bystanders. Problems with assays used to detect these antibodies are still evident but they remain widely utilized both to help establishing the diagnosis of SLE and to monitor the progress of the disease.

One of the main findings of the current study was increased levels of serum neopterin in SLE patients (active and inactive) compared to normal subjects, and in patients with active disease compared to inactive ones. Serum neopterin level showed higher sensitivity than other SLE markers (80%) and second highest specificity after anti-dsDNA antibodies (73%). These findings confirmed that there is a continuous low grade activation of the cellular immune system in patients with SLE even if the disease is inactive and without being associated with clinical symptoms. These findings were demonstrated by a study conducted by Leohiron et al.[37] who concluded that the correlation between neopterin concentration and evidence of disease activity was significant. They, also, reported that all patients with clinically active SLE had increased neopterin levels, and only 37.5% exceeded the upper normal limit of serum neopterin during clinical remission. Other studies reported that serum or urinary neopterin could discriminate active from inactive SLE patients[4, 29].

A recent study done by Mahmoud et al.[38] found that serum levels of neopterin, TNF-alpha and soluble tumor necrosis factor receptor II (sTNFRII) were significantly increased in patients with SLE, and they were the only parameters that showed significant higher levels in SLE patients with mild activity compared to normal subjects. They, also, reported that serum neopterin and sTNFRII could be used to identify SLE patients from normal subjects with a sensitivity and specificity of 100%, which suggested that serum levels of both parameters are more sensitive markers of disease activity than TNF-alpha, C3 or C4.

Jin et al.[39] suggested that increased lymphocyte apoptosis and defects in removal of apoptotic cells by macrophage contribute to the development of SLE. Serum levels of neopterin in active SLE patients were significantly higher than controls and correlated with the overall lupus disease activity. The increased levels of serum neopterin may be an attempt of the patients' macrophage system to remove the apoptotic cell excess. They concluded that serum neopterin may be regarded as an index of SLE disease activity.

In the present study, serum neopterin level showed a highly significant positive correlation with each of ESR, C3dg, and anti-dsDNA, and a significant negative correlation with both levels of C3 and C4.This agreed with the results of Lim et al.[3] who stated that ESR, serum complement level and neopterin are accepted as measures of disease activity in SLE and their changes are significantly different between

patients with active SLE and those with inactive disease. Nagy et al.[4] reported that neopterin level and anti-dsDNA provide together a very highly significant laboratory analysis model for SLE.

The present study demonstrated that serum neopterin level was significantly lower in active SLE patients receiving combined therapy of prednisolone and cytotoxic drugs compared to those receiving either prednisolone alone or cytotoxic drugs alone. Comparison of active SLE patients receiving prednisolone alone to those receiving cytotoxic drugs alone did not show any statistical significance. Thus, serum neopterin level can therefore be considered as a reflection of the treatment efficacy in suppressing disease activity.

Drugs, like steroids, affect the proportion of lymphocyte subpopulations and the expression of cell surface molecules and thus could potentially influence neopterin production[40]. This was agreed by Niederwieser et al.[41] and Prior et al.[42] who emphasized the same finding in their studied groups on other autoimmune diseases.

The current study demonstrated a significant increase in the serum neopterin levels in active SLE patients with multiple organ affection compared to those with single organ affection regardless the type of organ affected. This indicated that patients with multiple organ affection have generally a more active disease.

Mahmoud et al.[38] found significantly higher neopterin levels in SLE patients with membranous nephritis and with neuropsychiatric lupus erythematosus (NPLE) compared to patients without nephritis and NPLE. Also, patients with vasculitis had significant elevation of serum neopterin levels compared to patients without vasculitis.

In conclusion, the present results suggest that the estimation of serum neopterin levels seems beneficial in the assessment of disease activity and progress in SLE patients as well as the assessment of the efficacy of various treatment regimens used. However, further research is required with a larger sample group to establish the exact role of that marker in the pathogenesis of SLE.

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مستوى النيوبترين في مصل مرضى الذئبة الحمراء: علاقته بنشاط المرض وإصابة الأعضاء وأنظمة العلاج المختلفة

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إن التفرقة بين مرضى الذئبة الحمراء في طوري المرض النشط والخامل تعد من أكبر التحديات. كما أن التعرف على دلالات جديدة وحساسة لنشاط المرض سوف تكون لها أهمية كبيرة في علاج هذا المرض.

لذلك تهدف هذه الدراسة إلى إيجاد العلاقة بين مستويات النيوبترين في مصل الدم والعديد من القياسات الأخرى المستخدمة دائما في تحديد نشاط المرض، كما تهدف أيضا إلى تحديد مستويات النيوبترين في مصل

مرضى الذئبة الحمراء ومدى تأثره بإصابة أعضاء الجسم المختلفة، كذلك تحديد مستوياته أثناء تعاطي أنواع مختلفة من العلاج.

اشتملت هذه الدراسة على ٧٥ أنثى: ٢٦مصابة بمرض الذئبة الحمراء في الطور النشط، و ٢٤ مصابة بمرض الذئبة الحمراء في طوره الخامل و ٢٥ أنثى سليمة كمجموعة ضابطة. وقد أخذ في الاعتبار أن جميع مرضى الذئبة الحمراء الذي شملهم هذا البحث يجب أن تستوفي أربعة أو أكثر من المعايير الخاصة بمنظمة الروماتيزم الأمريكية، وقد تم تحديد نشاط المرض باستخدام الدلائل الخاصة بالمجموعة البريطانية لتقييم داء الذئبة الحمراء.

تم قياس كل من: سرعة الترسيب، مستويات البولينا والكرياتينين في مصل الدم، وظائف الكبد، المتممات المناعية الثالثة والرابعة، نواتج تكسير متممة المناعة الثالثة، والأجسام المناعية المضادة لحامض الدي أوكسي ريبونيوكليك ومستوى النيوبترين في مصل الدم.

أظهرت النتائج وجود زيادة ذات دلالة إحصائية في مستوى النيوبترين في مصل مرضى الذئبة الحمراء في الطور النشط مقارنة بالمجموعة المصابة بالمرض في الطور الخامل. كما وجدت زيادة ذات دلالة إحصائية في مستوى النيوبترين في مصل مرضى الذئبة الحمراء بطوريه عنه في المجموعة الضابطة. وقد تبين أن مستوى النيوبترين في مصل الدم يتمتع بأعلى حساسية تصل إلى ٨٠٪ مقارنة بدلالات المرض الأخرى، وهو ثاني أعلى تخصصية (٧٣٪) بعد الأجسام المناعية المضادة لحامض الدي أوكسي ريبونيوكليك. كذلك وجدت علاقة إرتباط طردية ذات دلالة إحصائية بين مستوى النيوبترين في مصل الدم وكل من: نواتج تكسير متممة المناعة الثالثة، والأجسام المناعية المضادة لحامض الدي أوكسي ريبونيوكليك وسرعة الترسيب. ومن جهة أخرى وجدت علاقة إرتباط عكسية ذات دلالة إحصائية بين مستوى النيوبترين في مصل الدم والمتممات المناعية الثالثة والرابعة. أما بالنسبة لمختلف أنظمة العلاج المستخدمة في داء الذئبة الحمراء في الطور النشط فقد وجد إنخفاض في مستوى النيوبترين في مصل المرضى اللاتي تعالجن بدواء البردنيزولون والأدوية السامة للخلايا معا مقارنة بالمرضى اللاتي تعالجن بدواء البردنيزولون وحده أو الأدوية السامة للخلايا وحدها. كما وجد اختلاف ذو دلالة إحصائية في مستوى النيوبترين في مصل المرضى المصابات بأعضاء متعددة عنهن في المرضى المصابات بعضو واحد بغض النظر عن العضو المصاب.

ومن هذه الدراسة يمكن استخلاص أن قياس مستوى النيوبترين في مصل الدم يبدو مفيدا في تقييم نشاط المرض وتقدمه في مرضى الذئبة الحمراء، وكذلك في تقييم الفائدة المرجوة من مختلف أنظمة العلاج.