Serum Protein Electrophoresis in Iraqi Systemic lupus Erythematous Patient

Zamin Abdulhussein Al-Sarray *[1]; Izzat Abdulsatar Al-Rayahi[2]; Ali H. Al-Hafidh[3] and Abbas T. Dwayyikh[4]

[(1)] Imamein Kadhimen Medical City, Ministry of Health and Environment Iraq

[(2)] Middle Technical University/ College of Health and Medical Technology, Baghdad - Iraq

[(3)] Physiotherapy Department, Middle Technical University College of Health and Medical Technology, Baghdad - Iraq

[(4)] Medical City, National Center for Teching Laboratories, Ministry of Health and Environment Iraq

E-mail (*): zamin87zn@gmail.com mobile :07713267233

Abstract

Background: Systemic lupus erythematosus (SLE) is a relapsing-remitting autoimmune disease with wide ranging organ involvement and clinical symptoms varying from mild and transient symptoms to death. Systemic lupus erythematosus typically develops between the teen and adult years, ranging from ages 15-44 years, predominantly affecting females in the reproductive age.

Objective: To find the relationship between serum protein electrophoresis levels and hematological parameters and the severity of SLE in Iraqi patients.

Patients and methods: the study involved a total of 40 SLE patients who attended one of Baghdad teaching hospitals from October 2018 until May 2019. Diagnosis of SLE was based on the criteria published by the American College of Rheumatology (ACR) for SLE classification and was subdivided depending on SLEDAI into SLE-S (29 sever) and SLE-M (11 moderate). SLEDAI was calculated for all patients (sever & moderate) as following: no activity (SLEDAI= 0), mild activity (SLEDAI 1-5), moderate activity (SLEDAI 6-10), high activity (SLEDAI 11-19), very high activity (SLEDAI ≥20). In addition, a total of 10 apparently healthy individuals and 10 RA patients were included in the study as a control group. Blood samples were collected from patients and control, and serum was separated. Serum protein electrophoresis and hematological parameters were measured in both patients and control. In addition, urine samples were collected in plastic disposable tubes, and labeled from study patients and control for urinary RBC count and protein urea (persistent proteinuria greater than +3 by dipstick) were detected.

Results: the study showed that the majority of patients (40%) were aged <20-29 years. A significant difference in the WBC count was noticed between SLE-S (5.10±2.33 10^9/L), SLE-M (4.90±2.63 10^9/L), RA (5.06±2.45 10^9 /L), and control (6.05±1.96 10^9 /L).

On the other hand, Monocyte count showed no significant difference between SLE-S (4.25±1.51%), SLE-M (3.94±1.60%), RA (3.89±1.38%), and control (4.05±0.72%). While other hematological parameter showed a highly significant difference between studied groups such as hemoglobin between SLE-S (10.97±1.45 g/dL), SLE-M (11.05±1.86 g/dL), RA (10.68±1.27 g/dL), and control (13.95±0.62 g/dL) , platelet between SLE-S (229.76±99.2 109/L), SLE-M (242.16±104.4 109/L), RA (412.57±124.6 109 /L), and control (315.70±73.78 109 /L), Lymphocyte between SLE-S (28.39±11.28 %), SLE-M(28.60±10.11%),RA (24.88±8.13 %),and control (39.57±5.82%). There was a significant difference in Neutrophils between SLE-S (60.52±15.64%), SLE-M (62.31±9.34%), RA (63.85±7.53%), and control (52.86±10.29%). Similarly, Eosinophils were significantly different between SLE-S (1.28±0.68%), SLE-M (1.41±0.65%), RA (1.54±0.77%), and control (2.49±1.32%); and Basophils were significantly different between SLE-S (0.75±0.29%), SLE-M (0.77±0.28%), RA (0.91±0.37%), and control (0.56±0.21%). Finally, a significant difference was noticed in ESR between SLE-S (59.60±36.19 mm/hr), SLE-M (51.79±37.33 mm/hr), RA (86.40±45.34 mm/hr), and control (7.86±1.97 mm/hr). Furthermore, distribution of studied groups by results of urine protein and hematuria showed a highly significant difference. Also a highly significant difference in serum albumin was noticed between SLE (35.3412 g/l) and control (41.486 g/l). In addition, a highly significant difference in the gama globulin was noticed between SLE (15.4442 g/l) and control (9.656 g/l).

Conclusion: decreased in serum albumin and increased in gamma globulin were found to be prevalent in SLE patients in our study. This decreased in serum albumin and increased in gamma globulin was related to proteinurea and disease score in SLE patients, and thus to disease activity.

Keywords: *SLE, S. protein electrophoresis, hematological parameters.*

الترحيل الكهربائي للبروتين المصلي لمرضى داء الذئب الاحمراري العراقيين

زمن عبدالحسين السراي [1] ، أ.د. عزة عبدالستار الرياحي [2] ، م.د.علي حسين فالح [3] ، تقني طبي عباس ثامر دويخ[4]

الخلاصة

الخلفية: داء الذئب الاحمراري (مرض الذئبة الحمراء) هو مرض المناعة الذاتية مع مشاركة واسعة النطاق للأعضاء والأعراض السريرية التي تتراوح من أعراض خفيفة وعابرة حتى الموت. تتطور الذئبة الحمامية الجهازية عادة بين سن العاشرة و البالغين ، وتتراوح أعمارهم بين 15 و 44 عامًا ، وتؤثر في الغالب على الإناث في سن الإنجاب.

الهدف:ايجاد العلاقة بين الترحيل الكهربائي للبروتين في الدم و المعلمات الدموية و فعالية داء الذئب الاحمراري بين المرضى العراقيين.

المرضى و طرق العمل: شملت الدراسة 40 مريض يعانون من الذئبة الحمراء المرضى الذين حضروا الى مستشفى بغداد التعليمي من أكتوبر 2018 حتى مايو 2019. استند تشخيص مرض الذئبة الحمراء (SLE) إلى المعايير التي نشرتها الكلية الأمريكية لأمراض الروماتيزم (ACR) لتصنيف مرض الذئبة الحمراء (SLE) وتم تقسيمها تبعًا ل SLEDAI إلى (SLE-S 29 شديد) و(SLE-M 11 معتدلة). تم حساب مؤشر SLEDAI لجميع المرضى على النحو التالي: لا يوجد نشاط (SLEDAI = 0) ، نشاط خفيف (SLEDAI 1-5) ، نشاط معتدل (SLEDAI 6-10) ، نشاط مرتفع (SLEDAI 11-19) ، نشاط مرتفع للغاية (SLEDAI ≥20). بالإضافة إلى ذلك ، تم تضمين مجموعه 10 أفراد يتمتعون بصحة جيدة و 10 مرضى RA في الدراسة كمجموعة سيطرة. تم جمع عينات الدم من المرضى و السيطرة ، وفصل المصل. تم قياس الترحيل الكهربائي للبروتين في الدم والمعلمات الدموية في كل من المرضى و السيطرة. بالإضافة إلى ذلك ، تم جمع عينات البول في أنابيب بلاستيكية ، وتمت تأشيرها من مرضى الدراسة والسيطرة لعد RBC البول والبروتين يوريا (بروتينية ثابتة أكبر من + 3 مقاس بواسطة اشرطة قياس) تم الكشف.

النتائج: أظهرت الدراسة أن غالبية المرضى (40 ٪) تتراوح أعمارهم بين 20-29 سنة. لوحظ وجود اختلاف كبير في عدد WBC بين (SLE-S (5.10 ± 2.33 10^9 /L)، (SLE-M 4.90± 2.6310^9 /L) RA (5.06 ± 2.45) 10^9/L ، والسيطرة .(6.05±1.96 10^9 /L) من ناحية أخرى ، لم يظهر عدد الكريات الأحادية اختلافًا كبيرًا بين SLE-S (4.25 ±1.51%)، SLE-M (3.94 ± 1.60%) RA (3.89 ± 1.38%) ، والسيطرة.(4.05±0.72%). بينما أظهرت المعلمات الدموية الأخرى فرقًا كبيرًا بين المجموعات المدروسة مثل الهيموغلوبين بين SLES(10.97±1.45 g/dL), SLE-M (11.05±1.86 g/dL), RA (10.68±1.27 g/dL),و السيطرة(13.95±0.62 g/dL))الصفائح الدموية بين SLE-S (229.76±99.2 10^9/L)، SLE-M (10^9/L 242.16 ± 104.4)، (412.57 ± 124.6 10^9/L) RA ، والسيطرة (315.70 ± 73.78 10^9/L) ، اللمفاويات بين SLE-S (28.39 ± 11.28%)، SLE-M (28.60 ± 10.11%)، RA (24.88 ± 8.13%) ، والسيطرة.(39.57±5.82%). كان هناك اختلاف كبير في العدلات بين SLE-S (60.52 ± 15.64%)، SLE-M (62.31±9.34%)، RA (63.85 ± 7.53%) ، والسيطرة .(52.86±10.29%). وبالمثل ، كانت الحمضات مختلفة بشكل كبير بين SLE-S (1.28 ± 0.68%)، SLE-M (1.41±0.65%)،RA (1.54 ± 0.77%) ، والسيطرة (2.49±1.32%) ؛ وكانت الخلايا القاعدية مختلفة بشكل كبير بين(SLE-S (0.75 ± 0.29 %)، SLE-M (0.77± 0.28%) RA (0.91 ± 0.37%) ، والسيطرة .(0.56±0.21%). أخيرًا ، لوحظ اختلاف كبير في ESR بين SLE-S (59.60±36.19mm/hr), SLE-M (51.79±37.33 mm/hr), RA(86.40±45.34mm/hr) و السيطرة (7.86±1.97 mm/hr)علاوة على ذلك ، أظهر توزيع المجموعات المدروسة حسب نتائج بروتين البول وبيلة دموية فرقًا كبيرًا للغاية. كما لوحظ وجود اختلاف كبير في زلال المصل بينSLE(35.3412g/L) والسيطرة (41.486 g/L). وبالإضافة إلى ذلك ، لوحظ وجود فرق كبير للغاية في الجلوبيولين كاما بين SLE (15.4442g/L) والسيطرة (9.656 g/L).

الاستنتاج: تم العثور على انخفاض في الزلال في المصل وزيادة في الجلوبيولين كاما كانت سائدة في مرضى الذئبة الحمراء في دراستنا هذا الانخفاض في المصل الزلال وزيادة في الجلوبيولين كاما كان مرتبطا بروتين يوريا ودرجة المرض في مرضى الذئبة الحمراء ، وبالتالي إلى نشاط المرض.

الكلمات المفتاحية : *داء الذئب الاحمراري الجهازي , الترحيل الكهربائي للبروتين في مصل الدم, المعلمات الدموية .*

Introduction

Systemic lupus erythematosus (SLE) is a complex multisystem, autoimmune disease likely resulting from an interaction between genetic and environmental risk factors [1]. It is characterized by diverse clinical phenotypes and various autoantibodies against nuclear components [2]. These auto antibodies include anti-DNA anti-n RNP, anti-Ro, anti-SM, and anti-La anti bodies, have been associated with HLA Class II gene [3]. Most organs can be involved in SLE and the typical major organ manifestations (e.g. from kidneys and the central nervous system) [4]. Organ damage over time caused by treatment-related complications and persistent disease activity is commonly associated with SLE [5]. Abnormalities of hematological system are very common in systemic SLE [6]. The inflammatory process in SLE involves inflammatory cells and molecules that cause changes in the number, shapes, and sizes of bone marrow cells and peripheral blood cells. SLE is characterized by B-cell activation and resultant autoimmunity with the production of numerous cytokines. Cytokines play a very important role in the pathogenesis of SLE. Neutrophils and platelets are involved in the production of these cytokines, which contribute to the activation of neutrophils and platelets. Leukocytes play a major role in inflammatory processes, and neutrophils are the most abundant type of leukocytes. Platelet activation is observed in patients with SLE. Lymphocyte count is usually decreased in SLE, and platelet count is decreased in SLE patients very often [7].

The hallmark of lupus glomerulonephritis is proteinuria and, at the present time, it is the principal urinary biomarker that is measured when screening for the disease. In fact, it is used in several validated scoring systems to measure disease activity, including the SLEDAI and the British Isles Lupus Assessment Group index [8]. Hematuria is described as the presence of red blood cells (RBCs) in the urine [9].

Human plasma is a complex solution which contains more proteins, probably hundreds, some of which are present in insignificant quantities. Serum proteins are represented mainly by albumin, globulins, and fibrinogen. Serum proteins perform multiple functions in the body, including: the role of carrier, transporting certain ions and molecules (lipids, hormones, vitamins); a role in controlling the activity of different proteolytic enzymes; a role in regulation of osmotic pressure and buffers [10].

SLE is the autoimmune disease with the largest diversity of detectable autoantibodies with more than 180 different specificities described, but only a few have been shown to be directly involved in tissue injury [11]. However, published investigations on human's most abundant protein in plasma, i.e., albumin, as an autoantigen are scarce. As a target of autoantibodies, albumin would not obviously fit with the hypothesis of an impaired clearance of

apoptotic cells as a trigger for the development of SLE. While albumin was found to protect human endothelial cells from apoptosis, an albumin overload has been shown to induce apoptosis in renal tubular cells [12].

Two factors influencing serum proteins in SLE are, firstly, the effect of the disease process, and, secondly, in those patients with nephropathy, the loss of protein in the urine [13]. A polyclonal "swell like" gamma elevation indicates an excess of immunoglobulins, i.e. hypergammaglobulinemia. Polyclonal gammopathies can occur with any reactive or inflammatory process, and they are usually associated with nonmalignant conditions. The most common causes are severe infections, acute late stage inflammation (acute hepatitis, pyelonephritis, interstitial nephritis), chronic inflammation, chronic infectious disease (chronically persistent hepatitis), autoimmune disease (collagenosis, rheumatoid arthritis, SLE, other connective tissue disease or lymphoma) [14].

Patients and Methods

This study included 40 SLE patients (based on clinical examination and laboratory results) attending the rheumatology unit of Baghdad Teaching hospital during the period from October 2018 until May 2019. Patients were classified into SLE-Sever (SLE-S) and SLE-Moderate (SLE-M) according to Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Blood samples were collected from each patients and sera were separated and stored at -20 °C for further investigation. Serum was also collected from (10) apparently healthy, age and gender matched individuals as healthy control, and (10) RA patients as patients control.
Serum protein was measured by electrophoresis (Helena, United Kingdom) following the manufacturer's instructions.

In addition, full clinical history of the patients were recorded. Hematological parameters were measured by Ruby (cell Dyn) (Abbott, USA). In addition, proteinuria was detected by dipstick (Chugdo, KOREA).

Furthermore, the existence of hematuria (> 5 erythrocyte per high-power field) was measured by microscope (OMAX, US).
This study was carried out after acquiring approval of the relevant ethical committee.
Statistical analysis was done using SPSS (version 24) and Graph Pad Prism 5.0. The data are expressed as means ± standard deviation (SD). The results were considered to be statistically significant when p value was equal or less than 0.05 performed by independent T test and two–way ANOVA.

Results

The age of SLE patients included in the study ranged from <20 to >50 years. The majority of patients (40%) were in the age group <20-29 years followed by 35 % in the age group 40 - >50 years and finally 25 % in the age group 30-39 years as shown in figure 1.

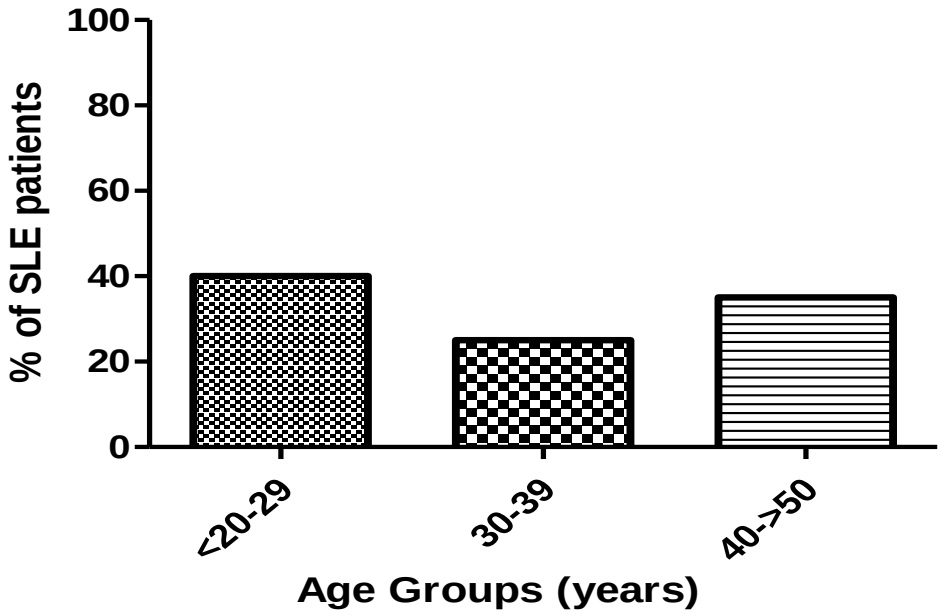

Figure (1): Distribution of patients according to age

Measurement of haematological parameters in the blood of patients and control showed that the mean of most haematological parameters was significantly lower in the SLE-S, SLE-M, RA patients than control. In addition, the mean of neutrophil and ESR increased in the SLE-S, SLE-M, RA patients compared to control with a highly significant difference between the studied groups ($p<0.0001$) as shown in table 1.

Table (1): Mean and Std. of the haematological parameters among studied groups

Parameters	SLE-S (n=29)	SLE-M(n=11)	RA(n=10)	Control(n=10)	p. value
WBC count (109 /L)	5.10±2.33	4.90±2.63	5.06±2.45	6.05±1.96	P<0.05 (S)
Hemoglobin (g/dL)	10.97±1.45	11.05±1.86	10.68±1.27	13.95±0.62	P<0.01 (HS)
platelet (109 /L)	229.76±99.2	242.16±104.4	412.57±124.6	315.70±73.78	P<0.01 (HS)
Lymphocyte count(%)	28.39±11.28	28.60±10.11	24.88±8.13	39.57±5.82	P<0.01 (HS)
Monocyte count(%)	4.25±1.51	3.94±1.60	3.89±1.38	4.05±0.72	P>0.05 (NS)
Neutrophils (%)	60.52±15.64	62.31±9.34	63.85±7.53	52.86±10.29	P<0.01 (HS)
Eosinophil (%)	1.28±0.68	1.41±0.65	1.54±0.77	2.49±1.32	P<0.01 (HS)
Basophil (%)	0.75±0.29	0.77±0.28	0.91±0.37	0.56±0.21	P<0.01 (HS)
ESR (mm/hr)	59.60±36.19	51.79±37.33	86.40±45.34	7.86±1.97	P<0.01 (HS)

S= significant, HS= highly significant, NS= non-significant

Blood was collected from patients and control and the hematological parameters was measured by Ruby (cell Dyn) and ESR was measured by Westergren method.

The existence of urine protein in the urine of patients and control showed that the higher percentage of positive urine protein was in SLE-S (72.41%), SLE-M (45.45%), RA (40%) than control group (0.0%) with a highly significant difference (P<0.01) as shown in Table 2.

Table (2): Distribution of studied groups by results of urine protein

Studied groups		Urine protein		Total
		Nil	Positive	
SLE-S	No.	8	21	29
	%	27.58%	72.41%	100.0%
SLE-M	No.	6	5	11
	%	54.54%	45.45%	100.0%
RA	No.	6	4	10
	%	60%	40%	100.0%
Control	No.	10	0	10
	%	100.0%	0.0%	100.0%

MCP< 0.01 (HS)

The existence of urine protein was measured by Urine dipstick in Patients and control serum. The existence of hematuria in the urine of patients and control showed that the higher percentage of positive urine protein in SLE-S (62.06%). SLE-M (27.27%) RA (39%) than control group (0.0%) with a highly significant difference (MCP< 0.01) as shown in Table 3.

Table (3): Distribution of studied groups by the results of Hematuria

Studied groups		Hematuria		Total
		Nil	Positive	
SLE-S	No.	11	18	29
	%	37.93%	62.06%	100.0%
SLE-M	No.	8	3	11
	%	72.72%	27.27%	100.0%
RA	No.	7	3	10
	%	70%	39%	100.0%
Control	No.	10	0	10
	%	100.0%	0.0%	100.0%

MCP< 0.01 (HS).

The mean level of serum albumin was lower in SLE patients (35.3412 g/l), than control group (41.486g/l). Globulin was higher in SLE patients (15.4442 g/l) than control (9.656 g/l) with a highly significant difference (MCP< 0.01) in serum albumin and gamma globulin between the SLE and control as shown in figure (2).

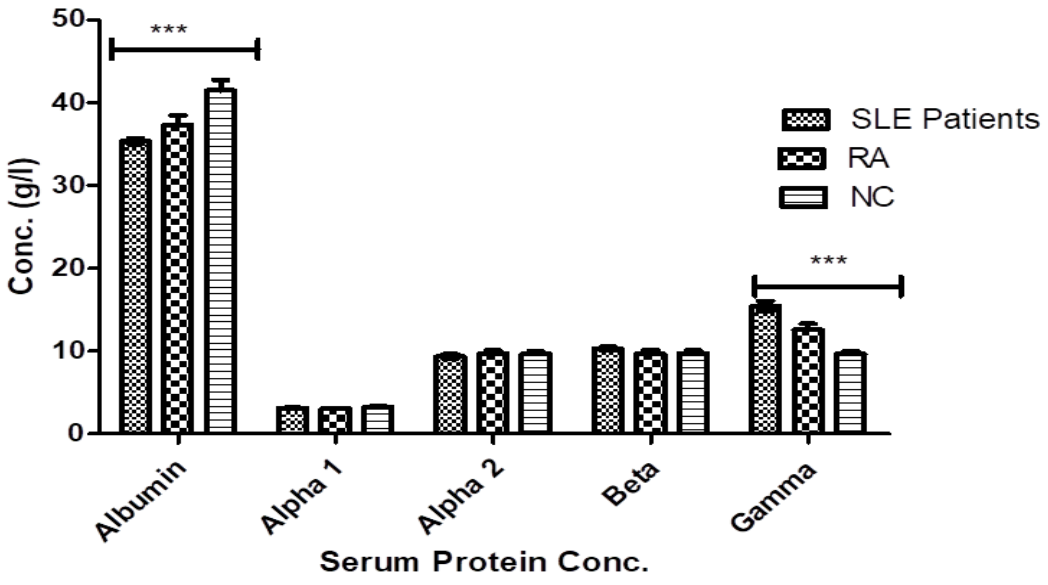

Figure (2): Mean level of serum protein (g/l) in the serum of patients and control

Blood was collected from patients and control and serum protein was measured by electrophoresis. Statistical analysis using two-way ANOVA showed a highly significant difference ** *in each of serum albumin and gamma globulin between SLE patients and control. Data are expressed as mean.

Discussion

Systemic lupus erythematosus (SLE) is a heterogeneous inflammatory chronic autoimmune disorder characterized by the deposition of immune complexes in different organs which may lead to multisystem involvement. It has a progressive as well as relapsing/remitting nature [15]. The disease More prevalent and more severe in Asian and African than in Europeans descents [16]. People of all genders, races, ancestral backgrounds, and ethnic groups can develop lupus [17]. It is most prevalent among women of childbearing age, but can occur in all ages. In about 10–20% of cases it begins before 16 years [18].

The age of SLE patients included in the study ranged from <20->50 years which is comparable to what has been previously reported [19]. Hematologic abnormalities, including anemia, thrombocytopenia (TCP), and leucopenia, are commonly found in SLE patients reflecting the activity of the disease over time [20]. Every tissue and cell in the body could be involved in SLE. The involved systems are hematological, musculoskeletal, cutaneous, renal, nervous system, vascular, pulmonary, gastrointestinal and ocular. Hematological manifestations are more frequent because blood and blood vessels together contain various numbers of antigens than any other organ in the body [21]. The principal of hematological abnormalities are anemia, leukopenia and thrombocytopenia [22]. The causes of cytopenia in SLE may be due to the presence of autoantibodies, Chronic inflammation, immunosuppressive drugs and marrow suppression [23, 24].

The erythrocyte sedimentation rate has value in detecting low-grade bone infection, and in monitoring some patients with SLE. The erythrocyte sedimentation rate is a surrogate marker of the acute phase reaction. During an inflammatory reaction, the sedimentation rate is affected by increasing concentrations of fibrinogen, the main clotting protein, and alpha globulins. The test mainly measures the plasma viscosity by assessing the tendency for red blood cells to aggregate and ‘fall’ through the variably viscous plasma [25].

In agreement with this proposal CBC and ESR were altered in SLE patients when compared to the control [21, 22].

Systemic lupus erythematosus can cause the body to produce antibodies directed against the kidney membranes. Normally, the filtering membranes do not permit albumin and other blood proteins to be lost in the urine. However, when systemic lupus attacks the kidney, the filtering membranes are disrupted, resulting in the finding of protein in the urine [26].In agreement with this proposal SLE patients positive urine protein when compared to the control [27, 28].

Potential alternative causes should be considered in cases of hematuria and pyuria. In female patients, urinalysis may be contaminated by red and white blood cells from menstruation. Urinary tract infections are among the most common infections in women, and can cause pyuria. This may be a particular concern in SLE a disease that in many patients is immunosuppressed therapeutically. Further urolithiasis is a common cause of hematuria, particularly among older male patients [29]. Low serum albumin levels have been frequently reported in SLE and are known to be associated with disease activity, particularly in patients with lupus nephritis [30]. In agreement with this proposal, the mean level of serum albumin was significantly less in the sera of SLE patients when compared to the control [30،32].

Serum albumin is routinely measured in patients with SLE as part of standard biochemical profiles. A low serum albumin level may be a result of increased albumin catabolism due to chronic inflammation and/or because of inadequate protein and caloric intake in patients with SLE. In addition, nephritis a common manifestation of SLE, may lead to nephrotic range proteinuria which in turn lowers serum albumin levels [31]. Systemic lupus erythematosus is characterized by elevated levels of gamma globulin and autoreactive antibodies [33]. In agreement with this proposal, the mean level of gamma globulin was significantly higher in the sera of SLE patients when compared to the control [34, 35].

Autoantibodies are central to the pathogenesis of SLE and are typically present many years before SLE is diagnosed [36]. It might therefore be expected that increased gamma globulin synthesis to produce these autoantibodies would increase serum globulin levels in patients with SLE [30].

To conclude

The results of the present study has demonstrated that decreased in serum albumin and increased in gamma globulin were prevelant in the majority of Iraqi SLE patients included in this study associated with higher disease activity.

References

1. Barbhaiya M, Costenbader KH. Environmental exposures and the development of systemic lupus erythematosus. Current opinion in rheumatology. 2016;28(5):497-505.

2. Chen L, Shi Z, Tan G, Han Y, Tang Z, Wang L. Systemic lupus erythematosus with and without a family history: a meta-analysis. Lupus. 2018;27(5):716-21.

3. Putterman C, Pisetsky DS, Petri M, Caricchio R, Wu AH, Sanz I, et al. The SLE-key test serological signature: new insights into the course of lupus. Rheumatology. 2018;57(9):1632-1640.

4. Bengtsson AA, Ronnblom L. Systemic lupus erythematosus: still a challenge for physicians. Journal of internal medicine. 2017;281(1):52-64.

5. Mok CC. Current role of rituximab in systemic lupus erythematosus. International journal of rheumatic diseases. 2015;18(2):154-163.

6. Beyan E, Beyan C, Turan M. Hematological presentation in systemic lupus erythematosus and its relationship with disease activity. Hematology. 2007;12(3):257-261.

7. Lee YH, Song GG. Association of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and mean platelet volume with systemic lupus erythematosus disease activity: a meta-analysis. Journal of Rheumatic Diseases. 2017;24(5):279-286.

8. Reyes-Thomas J, Blanco I, Putterman C. Urinary biomarkers in lupus nephritis. Clinical reviews in allergy & immunology. 2011;40(3):138-150.

9. Moreno JA, Sevillano Á, Gutiérrez E, Guerrero-Hue M, Vázquez-Carballo C, Yuste C, et al. Glomerular Hematuria: Cause or Consequence of Renal Inflammation? International journal of molecular sciences. 2019;20(9):2205.

10. Gurau G, Coman M, Dinu CA, Busila C, Voicu DC, Macovei LA, et al. The Electrophoretic Patterns of Serum Proteins in Children. Rev Chim. 2016;67:190-194.

11. Yaniv G, Twig G, Shor DB-A, Furer A, Sherer Y, Mozes O, et al. A volcanic explosion of autoantibodies in systemic lupus erythematosus: a diversity of 180 different antibodies found in SLE patients. Autoimmunity reviews. 2015;14(1):75-79.

12. Nehring J, Schirmbeck LA, Friebus-Kardash J, Dubler D, Huynh-Do U, Chizzolini C, et al. Autoantibodies against albumin in patients with systemic lupus erythematosus. Frontiers in immunology. 2018;9.

13. Carlsson A, Wuttge DM, Ingvarsson J, Bengtsson AA, Sturfelt G, Borrebaeck CA, et al. Serum protein profiling of systemic lupus erythematosus and systemic sclerosis using recombinant antibody microarrays. Molecular & cellular proteomics. 2011;10(5):M110.

14. Regeniter A, Siede W. Peaks and tails: Evaluation of irregularities in capillary serum protein electrophoresis. Clinical biochemistry. 2018;51:48-55.

15. Talaat RM, Mohamed SF, Bassyouni IH, Raouf AA. Th1/Th2/Th17/Treg cytokine imbalance in systemic lupus erythematosus (SLE) patients: Correlation with disease activity. Cytokine. 2015;72(2):146-153.

16. Shaikh MF, Jordan N, D'Cruz DP. Systemic lupus erythematosus. Clinical medicine (London, England). 2017;17(1):78-83.

17. Danchenko N, Satia J, Anthony M. Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. Lupus. 2006;15(5):308-318.

18. Fonseca R, Aguiar F, Rodrigues M, Brito I. Clinical phenotype and outcome in lupus according to age: a comparison between juvenile and adult onset. Reumatología Clínica (English Edition). 2018;14(3):160-163.

19. Watad A, Mahroum N, Whitby A, Gertel S, Comaneshter D, Cohen AD, et al. Hypothyroidism among SLE patients: case–control study. Autoimmunity reviews. 2016;15(5):484-486.

20. Abdel Galil SM, Edrees AM, Ajeeb AK, Aldoobi GS, El-Boshy M, Hussain W. Prognostic significance of platelet count in SLE patients. Platelets. 2017;28(2):203-207.

21. Abira M, Akhter QS. Relationship between CBC and ESR and duration of disease in patients with systemic lupus erythematosus (SLE). Journal of Bangladesh Society of Physiologist. 2018;13(2):41-46.

22. Aleem A, Al Arfaj AS, Khalil N, Alarfaj H. Haematological abnormalities in systemic lupus erythematosus. Acta Reumatol Port. 2014;39(3):236-241.

23. Fayyaz A, Igoe A, Kurien BT, Danda D, James JA, Stafford HA, et al. Haematological manifestations of lupus. Lupus science & medicine. 2015;2(1):1-18.

24. Njoroge J, Oyoo G, Kitonyi G, Barasa A, Odhiambo A. Haematological parameters in systemic lupus erythematosus patients at Kenyatta National Hospital, Nairobi. African Journal of Rheumatology. 2016;4(2):57-62.

25. Harrison M. Abnormal laboratory results: Erythrocyte sedimentation rate and C-reactive protein. Australian prescriber. 2015;38(3):93.

26. Cojocaru M, Cojocaru I, Silosi I, Vrabie C. Kidney damage in autoimmune diseases. Journal of Medical Biochemistry. 2010;29(2):61-65.

27. Schäfer V, Weiß K, Krause A, Schmidt W. AB0539 Does erythrocyte sedimentation rate reflect disease activity in patients with systemic lupus erythematodes? correlation with acute phase reactants, immunological parameters and proteinuria. BMJ Publishing Group Ltd; 2017. p. 1239-1240.

28. Nazri SKS, Wong KK, Hamid WZW. Pediatric systemic lupus erythematosus: Retrospective analysis of clinico-laboratory parameters and their association with Systemic Lupus Erythematosus Disease Activity Index score. Saudi medical journal. 2018;39(6):627.

29. Ding JY, Ibañez D, Gladman DD, Urowitz MB. Isolated hematuria and sterile pyuria may indicate systemic lupus erythematosus activity. The Journal of rheumatology. 2015;42(3):437-440.

30. Kwon OC, Lee JS, Ghang B, Kim Y-G, Lee C-K, Yoo B, et al., editors. Predicting eventual development of lupus nephritis at the time of diagnosis of systemic lupus erythematosus. Seminars in arthritis and rheumatism. Elsevier. 2018;48(3):462-466.

31. Yip J, Aghdassi E, Su J, Lou W, Reich H, Bargman J, et al. Serum albumin as a marker for disease activity in patients with systemic lupus erythematosus. The Journal of rheumatology. 2010;37(8):1667-1672.

32. Li Z, Xu D, Wang Z, Wang Y, Zhang S, Li M, et al. Gastrointestinal system involvement in systemic lupus erythematosus. Lupus. 2017;26(11):1127-1138.

33. Baum CG, Chiorazzi N, Frankel S, Shepherd GM. Conversion of systemic lupus erythematosus to common variable hypogammaglobulinemia.The American journal of medicine. 1989;87(4):449-456.

34. Schurder J, Goulenok T, Jouenne R, Dossier A, van Gysel D, Papo T, et al. SAT0293 Pneumococcal infection in patients with systemic lupus erythematosus. BMJ Publishing Group Ltd; 2017. p. 883-884.

35. Wu L, Wang X, Chen F, Lv X, Sun W, Guo Y, et al. T cell subsets and immunoglobulin G levels are associated with the infection status of systemic lupus erythematosus patients. Brazilian Journal of Medical and Biological Research. 2018;51(2).

36. Arbuckle MR, McClain MT, Rubertone MV, Scofield RH, Dennis GJ, James JA, et al. Development of autoantibodies before the clinical onset of systemic lupus erythematosus. New England Journal of Medicine. 2003;349(16):1526-1533.