Figure 1. Serum level of IL-8 decreased significantly 3 months after additional HCQ treatment.

Figure 2. Correlation between the change of IL-8 and that of S100A8 protein ($r=0.51$, $p=0.044$).

Results: We enrolled 44 patients. Prednisolone dose during this study was fixed at the mean of 5.0 ± 2.9 mg per day. SELENA-SLEDAI scores, CLASI scores, anti-dsDNA antibody and serum levels of C3 improved significantly, and serum levels of S100A8 and S100A9 proteins decreased significantly 3 months after additional HCQ treatment. The changes in serum S100A8 and S100A9 levels in SLE patients with LN were more significantly higher than in those without LN.

Among these patients, the changes of serum cytokine expressions were measured in 18 patients. The expressions of IFNs were not detected in almost of all patients. Serum levels of TNF- α , IL-6, IL-8, IL-1 β , IL-1ra, VEGF, CCL3 and CCL4 decreased significantly 3 months after additional HCQ treatment (Figure1).

Seven of 18 SLE patients had a history of LN. These patients have been in sustained complete remission(CR) of LN for over one year(mean duration of CR was 5.0 ± 3.5 years).

The reductive effect of additional HCQ treatment on serum S100A9, TNF- α , IL-6 and IL-8 levels was much more apparent in those with history of LN (LN: S100A9, $p=0.016$, TNF- α , $p=0.016$, IL-6 $p=0.031$, IL-8, $p=0.031$; no LN: S100A9, $p=0.065$, TNF- α , $p=0.083$, IL-6 $p=0.090$, IL-8, $p=0.557$). The changes of serum S100A8 and S100A9 levels were correlated with those of serum IL-8 and IL-1ra (Figure2).

Conclusion: HCQ could reduce the serum levels of S100 protein and several cytokines in SLE Japanese patients with low disease activity. Recently, some reports showed that novel biomarker including IL-8 or S100 proteins was correlated with severity of LN [1, 2]. Our findings suggest that HCQ treatment without any additional immunosuppressant could reduce the expression of serum S100 proteins, IL-8 and IL-1ra, which were considered to be associated with the improvement of renal and life prognosis. Our data also indicated that S100 protein is closely related to IL-8 or IL-1ra expression in SLE pathogenesis, especially in LN. Farther investigations are needed to more clarify the significance of HCQ treatment in SLE.

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AB0488

RITUXIMAB THERAPY IN LUPUS NEPHRITIS RESISTANT TO CONVENTIONAL THERAPY – A SINGLE CENTER EXPERIENCE (CASE SERIES)

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Background: Lupus nephritis(LN) can be a cause of morbidity and mortality in a significant portion of patients. The treatment of lupus nephritis can be challenging in some patients who are resistant to conventional immunosuppressive treatment.

Objectives: Rituximab is a promising agent for treating resistant patients. We evaluated the response of lupus nephritis patients who were treated with rituximab treatment in our clinic retrospectively.

Methods: We evaluated LN patients who were followed and treated with at least one course of rituximab in our clinic between 2013-2018. Remission was defined as proteinuria below 500 mg/day. Also, we evaluated the reason behind the cessation of rituximab during the follow-up whether it is a side effect or lack of efficacy. A final 24-hour proteinuria level was also analyzed at the end of the follow-up.

Results: 33 patients (20 F, 13 M) were treated with rituximab. All patients had active lupus nephritis at initiation. Mean of disease duration was 6.7 years. Diagnosis was proven by renal biopsy, except two (Table). Patients received an average of 4.2 courses. All patients were treated with high dose steroids. The other medications, the patients were previously treated with, were Cyclophosphamide (n=26), Azathioprine (n=7), Mycophenolate mofetil (n=17). Also one patient was treated with plasmapheresis due to thrombotic thrombocytopenic purpura. 2 patients were lost in follow-up. 13 patients (39%) are still on rituximab. Six of them (46%) still have active LN. Among 18 patients in whom rituximab therapy was terminated, 3 had inadequate response, 2 had severe infection (cellulitis, pneumonia), 1 had Rituximab-induced serum sickness, 1 had will of pregnancy. Treatment of 11 patients was terminated owing to remission of disease. All of the patients whom rituximab was terminated in disease remission did not flare, except one. The mean level of pre-treatment proteinuria was 3356 ± 2478 mg/day. The mean level of proteinuria after the final course was 1025 ± 982 mg/day ($p<0.0001$). Mean erythrocyte sedimentation rate (ESR) was reduced from $28,62 \pm 22,95$ mm/h to $14,97 \pm 12,32$ mm/h ($p<0,005$). While initial steroid dose was $24 \pm 19,3$ mg/day, steroid dose at last rituximab course was $7,84 \pm 6,13$ mg/day ($p<0.0001$). None of the patients had a new organ involvement during therapy. End stage renal disease was developed in 3 patients. During the treatment 7 patients had infections, 2 had herpes zoster, 1 had cellulitis, 3 had pneumoniae and 1 had frequent upper respiratory infections.

Table. Histological characteristics of patients

RPS/ISN Classification	Number of patients
Class II	1
Class III	4
Class IV	11
Class V	7
Class III+IV	6
Class IV+V	2

Conclusion: In lupus nephritis patients resistant to conventional therapy, rituximab can be tried as an alternative treatment choice. In our single center, most of the patients were class IV nephritis whom we observed the efficacy of rituximab. Generally, the side effects were acceptable. Rituximab can be a steroid sparing agent in these patients.

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

AB0489 HYPONATREMIA AS AN INFLAMMATORY MARKER OF LUPUS DISEASE: FACT OR FAD

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Background: Premature atherosclerosis is clearly described in systemic lupus erythematosus as a main cause of poor outcomes and mortality(1). The pleiotropic adipokines including adiponectin and visfatin are implicated in the inflammatory process of lupus disease that promote the interleukins and cytokines signaling leading accelerated endothelial disruption(2)

Objectives: To evaluate the endothelial dysfunction by measuring serum Visfatin, adiponectin, leptin and HOMA-insulin Index as reliable biomarkers of the atherosclerosis & by estimating the FMD of brachial artery among lupus patients and correlating these parameters with clinical characteristics.

Methods: A case-control study in which 150 systemic lupus patients who were fulfilling American College of Rheumatology revised classification were recruited consecutively from Internal Medicine department at Cairo University, They were compared to 90 age & sex matched healthy controls. Patients who were pregnant, smoker, diabetic, those with hepatic and renal dysfunction, hypothyroidism, and familial dyslipidemia were excluded. Adiponectin, leptin, visfatin and HOMAIR were evaluated. Flow mediated dilatation of brachial artery was calculated as the maximum percent increase in artery diameter after cuff release compared to baseline

Results: The data revealed elevated levels of adiponectin, leptin, visfatin and HOMA IR in lupus cases compared to controls with reduced FMD percent. Clinical and laboratory background are summarized in table (1).

Table 1

Characteristics	Cases N=150	Controls N=90	p-value
Age(yr)	25.15±5.78	24.84±5.84	0.256
Female(N.%)	125 (84.66%)	65(73%)	0.34
Male(N.%)	25(16.44%)	25(27%)	
Disease duration in months	10±6		
BMI(Kg/m2)	25.56±3.66	22.74±2.13	<0.001
Clinical characteristic(N.%)	60(40%)		
- Mucocutaneous	123(82%)		
- Arthritis/arthritis	100(75%)		
- Renal disease	12(8%)		
- Central nervous disease	68 (41.5%)		
- Cardiovascular disease	49(32.66%)		
- Vascular occlusion			
Lab characteristics	97±8	89±4	<0.001
Fasting glucose(mg/dl)	10.6±2.9	12.8±0.7	<0.001
Hemoglobin% (gm/dl)	126±59	94±18	<0.001
Triglycerides (mg/dl)	187±44	143±8	<0.001
Total Cholesterol(mg/dl)	118.2±33.7	64.6±7	<0.001
LDL(mg/dl)	48±14	49±3	0.138
HDL(mg/dl)	42±11	4±3	<0.001
ESR (mm/hr)			
HOMA IR	10.6±5.2	4.0±0.3	<0.001
Plasma Adiponectin (ng/ml)	16.5±3.2	12.2±0.3	<0.001
Serum Leptin(ng/ml)	25.4±10.7	7.8±0.5	<0.001
Serum Visfatin (ng/ml)	18.0±5.6	10±1.5	<0.001
FMD of brachial artery%	8.82±1.99	11.60±1.2	<0.001

None of adipokines is correlated to age, BMI, Disease duration or activity. There is an inverse correlation between FMD of the brachial artery and total cholesterol, visfatin, adiponectin, leptin and HOMAIR (r-value= - 0.523, - 0.35, - 0.27, -0.45, -0.56 respectively) with P <0.05. Adipokines and FMD did not differ regarding clinical presentations especially cardiovascular. Roc curve analyses studied the performance of adipokines. Adiponectin and visfatin are better to predict reduced FMD.

Table 2

Variable	AUC	Cut-off point	P value	Sensitivity	Specificity	Asymptotic 95% CI
Homatet IR	0.466	12.15	0.718	50.7%	50.0%	0.268 0.663
Plasma Adiponectin	0.890	15.85	0.000	82.1%	80.0%	0.827 0.952
Serum Leptin	0.139	5.45	0.000	22.9%	20.0%	0.059 0.218
Serum Visfatin	0.890	17.50	0.000	82.1%	80.0%	0.828 0.952

Conclusion: Endothelial dysfunction is evident in SLE.Reduced FMD of brachial artery and increased adipokines and HOMAIR are noted. Adiponectin and visfatin could be predictors of atherosclerosis in lupus.

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AB0490 FIBROBLAST GROWTH FACTOR-23 IN SYSTEMIC LUPUS ERYTHEMATOSUSPATIENTS

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects multiple organs including the kidneys and the heart. Chronic kidney disease (CKD) is common among SLE patients. SLE is also associated with increased left ventricular (LV) mass. LV hypertrophy (LVH) may have an additional role in the increased morbidity and mortality among in SLE patients. Fibroblast growth factor 23 (FGF23) is a phosphatonin that steadily increases in serum of CKD patients. High FGF23 is associated with inflammation, CKD progression, and LVH.

Objectives: The aim of this study is to determine the serum level of FGF23 in SLE patients with and without lupus nephritis looking for its possible association with the inflammatory and cardiovascular manifestations encountered in this disease.

Methods: Sixty SLE patient were recruited and appointed into 2 groups based on renal function; group I composed of thirty patients that had normal kidney functions or stage 1 CKD (eGFR>90 ml/min/1.73m²) and group II of thirty cases with significant renal involvement defined as stage 2 to 4 CKD (eGFR <90 - >15 ml/min/1.73m²). After history taking and complete clinical examination of every patient, we measured body weight, height, Systemic lupus erythematosus disease activity index (SLEDAI), Systemic lupus erythematosus International Collaborating Clinics (SLICC), serum level of creatinine, calcium, phosphorus, albumin, complement 3 (C3), complement 4 (C4), interleukin 6 (IL6), fibroblast growth factor 23 (FGF23), estimated glomerular filtration rate (eGFR), 24 hour urine protein, complete blood count, erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), and left ventricular mass index (LVMI). Sixty normal healthy adults were included as control group. They were tested for serum FGF23 level.

Results: Serum level of FGF23 in SLE patients was comparable to normal control subjects (99.6±79.86 vs. 139±12.3 pg/mL,P>0.05). In addition, there was no significant difference in FGF23 between the two studied groups (106.49± 88.2 vs. 93.84± 74.67 pg/mL,P>0.05). In addition, there was no significant difference in serum IL6 between the two groups (58.6 ± 63.69 vs 55.9 ± 47.97 ng/L, P=085). On the other hand, LVMI was significantly higher in Group II(138.6 ± 36.59 vs. 187.6 ± 81.7 gm/m² in group I vs. group II respectively, P=0.0045). FGF23 showed significant positive correlation with IL6 (r= 0.776, P<0.001) and failed to show significant correlation with LVMI, serum creatinine, eGFR or serum phosphorus.

Conclusion: FGF23 behaves differently in SLE patients; in spite of significant increase in inflammation and the frequent renal involvement, FGF23 level remains normal in SLE patients. There is a possible existence of an inhibitor to FGF23 production in SLE. This possibility should trigger further studies.

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