Original Article

Predictive Value of Serum and Urinary Adiponectin in Systemic Lupus Erythematosus Activity and Lupus Nephritis

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by chronic inflammation. Lupus nephritis is a severe manifestation of SLE affecting about 50% of SLE patients with high morbidity and mortality. Adiponectin has anti-inflammatory properties. Adiponectin could be a factor linking inflammation in SLE and lupus nephritis (LN). **Aim of the Work:** To assess the level of serum & urinary adiponectin in SLE patients and to detect any relation between serum & urinary adiponectin levels and SLE activity and lupus nephritis. **Subjects and Methods:** This study included 30 female SLE patients and 15 female age matched healthy controls. SLE patients were subjected to full history taking, clinical examination and laboratory investigations of SLE & LN. Disease activity and renal involvement were assessed using SLE Disease Activity Index (SLEDAI) and Renal SLEDAI respectively. Patients were divided into active versus inactive and LN versus non-LN. Renal biopsies were taken from LN subgroup. Serum & urinary levels of adiponectin were measured using enzyme-linked immunosorbent assay (ELISA) in all subjects. **Results:** Significantly higher serum & urinary adiponectin level was found in SLE patients when compared with controls. Significantly higher serum & urinary adiponectin level was found among active SLE patients when compared with inactive patients as well as among patients with LN when compared to patients without LN. Significantly higher serum & urinary adiponectin level was found among inflammatory LN class (III & IV) patients when compared to non-inflammatory LN class (I & II). Serum & urinary adiponectin had a significant positive correlation with SLEDAI, renal SLEDAI, ESR 1st hour, proteinuria , anti-ds (DNA) titre and LN class while inverse correlation with C3 titre and C4 titre , also inverse correlation between urinary adiponectin and creatinine clearance were observed. **Conclusion:** Serum & urinary adiponectin levels are elevated in SLE patients and strongly associated with lupus activity & LN, so they may consider promising biomarkers for prediction of SLE activity & renal involvement especially urinary adiponectin in lupus nephritis. **[Egypt J Rheumatology & Clinical Immunology, 2014; 2(1): 53-62]**

Key Words: Systemic lupus erythematosus, adiponectin, lupus nephritis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is chronic autoimmune, multisystemic, relapsing, and remitting disease that is characterized by the production of autoantibodies directed against several antigens in multiple organs including joints, skin, serous membranes, kidneys, blood, central nervous system (CNS) and others organs[1,2].

Renal involvement is very common in SLE affecting 50% adult subjects suffering from SLE[3]. Lupus nephritis (LN) is a severe manifestation of SLE, caused in most cases by the glomerular deposition of anti-dsDNA antibodies that locally activate complement, and elicit a strong inflammatory response[4]. LN may be presented by a wide range of abnormalities ranging from asymptomatic proteinuria or microscopic hematuria with normal renal function, to severe nephrotic syndrome or renal failure[5]. Kidney biopsy may help to confirm the diagnosis, as well as providing useful view for the prognosis and decisions regarding therapy[6]. American College of Rheumatology (ACR) guidelines suggest that a kidney biopsy be performed when there are persistent abnormalities in the urinary sediment or increased serum creatinine[7].

Adiponectin, is adipocytokine 244-amino acid (30-kDa) protein secreted predominantly by white adipose tissue closely linked to components of the metabolic syndrome and is structurally similar to complement component C1q[8]. Adiponectin present in many forms, the monomeric form of adiponectin seems to occur only in the adipocyte, whereas oligomeric complexes circulate in plasma as low molecular weight trimers (LMW), middle molecular weight hexamers (MMW), and high molecular weight

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multimers (HMW)[9]. The adiponectin gene is located on chromosome 3q27, a region associated with susceptibility for developing metabolic syndrome and type 2 diabetes. Polymorphisms of the adiponectin gene may be associated with alterations of adiponectin function and important clinical conditions[10].

Adiponectin has anti-inflammatory and antiatherosclerotic properties on endothelial cells by decreasing vascular inflammation, foam cell formation, and cell adhesion, which all are involved in the initiation and progression of vascular lesions[8]. Adiponectin inhibits tumour necrosis factor alpha (TNF-α) and interlukin-6 (IL-6) production, also both TNF-α and IL-6 suppress adiponectin production, which suggests the existence of a negative feedback between adiponectin and pro-inflammatory cytokines[11]. Adiponectin had a role in acute kidney injury in experimental animals [(12)]. A small number of studies had examined adiponectin in patients with kidney disease & showed patients with end-stage kidney disease had elevated circulating levels of adiponectin [(13)]. Plasma adiponectin was found to be markedly elevated in patients with nephrotic syndrome, and this was independent of glomerular filtration rate[14]. Finally, increased serum adiponectin levels predict the progression from macroalbuminuria to end stage renal disease in type 1 diabetic patients[15].

The aim of this study was to assess the level of serum & urinary adiponectin in SLE patients and to detect any relation between serum & urinary adiponectin levels and SLE activity and lupus nephritis.

SUBJECTS AND METHODS

Subjects

The present study was carried out on 30 female patients with SLE fulfilling at least 4 criteria of the 11 the updated (ACR) criteria[16], they were selected from the internal medicine department in and out-patient in Tanta University Hospitals. 15 female age matched healthy subjects were also included in the study as control group. Consent was obtained from all subjects after full explanation of benefits and risks of the study.

Exclusion criteria

Patients with diabetes mellitus, high blood pressure (≥ 180/110), dyslipidemia, obesity (BMI ≥ 30), metabolic syndrome, heart failure, malignancies, overlap syndrome (coexistence of lupus with other connective tissue diseases), pregnancy, renal disease from any cause else, liver disease, documented infection within the last 2 weeks or patients on hemodialysis were excluded.

Methods

- Full history taking including disease duration & symptoms of SLE activity.
- Clinical examination of the patients including the following:
  1. Body mass index (BMI) was determined by Quelet index (weight by kg/height square by m^2).
  2. Assessment of the disease activity using SLE disease activity index (SLEDAI) which is a validated model for clinicians for the assessment of disease activity in SLE patients. SLEDAI consists of 24 variables with weighted score for each variable. The maximum possible score is 105; patients with active disease have 8 or more points[17].
  3. Lupus nephritis was assessed with the renal SLE disease activity index (renal SLEDAI) which consists of the 4 kidney related items including hematuria (>5 red blood cells/high power field), pyuria (>5 white blood cells/high power field), proteinuria (>0.5 g/24 hours or urine protein/creatinine ratio >0.5) and urinary casts. Each item in renal SLEDAI was assigned 4 points. Thus the scores for the renal SLEDAI can range from 0 to 16. Patients were diagnosed to have lupus nephritis if (renal SLEDAI score ≥ 8) or when proteinuria was the renal-related criterion, a renal SLEDAI score of 4.[17]

Laboratory assessment (for SLE patients)

1- Complete blood count.
2- Erythrocyte sedimentation rate (ESR) 1st hour using Westergren method.
3- C-reactive protein (CRP) using latex agglutination method.
4- Kidney function tests: urine analysis, serum creatinine and creatinine clearance.
5- Protein in 24 hours urine collection.
6- Quantitative determination of antinuclear antibody (ANA) and IgG autoantibodies to double-stranded DNA (anti dsDNA) by immunoassay (corgenix Inc and Orgentec Diagnostika GmbH respectively).
7- Serum complements C3 and C4 (assessed by nephelometry).
8- Serum and urine adiponectin were measured in SLE patients & the control groups using specific enzyme-linked immunosorbent assay (ELISA) according to manufacturer's directions (R & D Systems, Minneapolis, MN, USA). Urine adiponectin levels were standardized to urine creatinine measured in the same spot urine and expressed as µg/g creatinine. The fresh urine

samples were centrifuged to remove sediment and supernatants frozen in small aliquots without further manipulation at −20°C for later analysis. Plasma samples were also stored in aliquots at −20°C. samples had to be taken at the time of the renal biopsy ± 7 – days.

Renal biopsy was performed to SLE patients with renal involvement. The renal biopsy was examined by the same histopathologist and the results of biopsy were classified according to (International Society of Nephrology/ Renal Pathology Society ISN/RPS 2004 classification of Lupus Nephritis)[5].

Statistics

Statistical presentation and analysis of the present study was conducted, as continuous data were expressed as mean ± standard deviation. Comparison of continuous data between two groups was made by using unpaired t for parametric data and Mann-Whitney tests for nonparametric data. Spearman & Pearson tests for correlations between different parameter (nonparametric & parametric respectively) were used. ROC curve were used for estimation of sensitivity, specificity, cut off level, positive predictive value and negative predictive value. Probability (P) values of less than 0.05 were considered statistical significant, if less than 0.01 were considered statistical highly significant & if more than 0.05 were considered statistical not significant. Analyses were performed using SPSS program, version 19 (SPSS Inc., Chicago, IL, USA).

RESULTS

This study included 30 female patients with SLE; their ages ranged from 15 to 32 years (mean 21.84±4.909), 19 active SLE patients (63.33%) with their SLEDAI ≥ 8 while the other 11 patients (36.67%) were inactive (SLEDAI < 8) and 15 patients (50%) had lupus nephritis (renal SLEDAI score ≥ 8) while 15 patients (50%) had no lupus nephritis (renal SLEDAI score < 8). Renal biopsy revealed 8 patients had inflammatory LN classes (III & IV) and 7 patients had non-inflammatory LN classes (I & II). The other laboratory data of the patients were shown in (Table 2).

This study also included 15 healthy female; their ages ranged from 17 to 32 years (mean 23.4±4.421). Comparison between SLE patients & the control subjects were shown in (Table 3).

Our results showed higher serum adiponectin level was found in SLE patients (mean 16.98±5.356 µg/ml) when compared with controls (mean 7.92±1.629 µg/ml) with statistically highly significant difference (P<0.0001). Also higher urinary adiponectin level was found in SLE patients (mean 7.95±3.938 µg/g creatinine) when compared with controls (mean 2.73±0.3911 µg/g creatinine) with statistically highly significant difference (P <0.0001) (Table 3).

In the present study, Higher serum adiponectin level was found among SLE patients with LN (mean 19.997±5.999 µg/ml) when compared with SLE patients without LN (mean 13.97±1.995 µg/ml) with statistically significant difference (P=0.0235) (Figure 1). Higher urinary adiponectin level was found among SLE patients with LN (mean 10.94±3.4 µg/g creatinine) when compared with SLE patients without LN (mean 4.97±1.204 µg/g creatinine) with statistically highly significant difference (P<0.0001) (Figure 1). Other demographic and laboratory parameters comparing between SLE patients with LN & SLE patients without LN were shown in (Table 4).

Our results showed higher serum adiponectin level was found among active SLE patients (mean 19.09±5.6 µg/ml) when compared with inactive patients (mean 13.34±1.935 µg/ml) with statistically highly significant difference (P = 0.0004) (Figure 1). Also higher urinary adiponectin level was found among active SLE patients (mean 9.50±4.146 µg/g creatinine) when compared with inactive patients (mean 5.28±1.271 µg/g creatinine) with statistically highly significant difference (P=0.0004) (Figure 1). Other demographic and laboratory parameters comparison between active & inactive SLE patients were shown in (Table 4).

In the present study, Higher serum adiponectin level was found among inflammatory LN class (III & IV) patients (mean 23.73±4.821 µg/ml) when compared with non-inflammatory LN class (I & II) (mean 15.73±4.130 µg/ml) with statistically highly significant difference (P=0.0059). Higher urinary adiponectin level was found among inflammatory LN class (III & IV) patients (mean 13.67±1.796 µg/ml) when compared with non-inflammatory LN class (I & II) (mean 7.82±1.398 µg/ml) with statistically highly significant difference (P<0.0001) (Table 5).

In our SLE patients, Serum adiponectin had a significant positive correlation with SLEDAI (r=0.7282, P<0.0001) (Figure 2), renal SLEDAI (r=0.5176, P=0.0034) (Figure 3), ESR 1st hour (r=0.6889, P<0.0001), proteinuria (r=0.4535, P=0.0118), anti-ds (DNA) titre (r=0.6435, P<0.0001) and LN class (r=0.5480, P=0.0344), while inverse correlation with C3 titre (r= -0.6343, P=0.0002) and C4 titre (r=-0.7414, P=0.0004) were recorded. Also serum adiponectin had a significant positive correlation with urinary adiponectin in SLE patients (r=0.4185, P=0.0214). On the other hand non-significant correlations between serum adiponectin and other demographic and laboratory parameters were recorded (Table 6).

Also in our SLE patients, urinary adiponectin had a highly significant positive correlation with SLEDAI (r=0.5940, P=0.0005) (Figure 2), renal SLEDAI (r=0.8331, P<0.0001) (Figure 3), ESR 1st hour (r=0.5915, P=0.0006), proteinuria (r=0.7163, P<0.0001), anti-ds (DNA) titre (r=0.4581, P=0019) and LN class (r=0.7749, P=0.0007), while inverse correlation with creatinine clearance (r=-0.5122, P=0.0038), C3 titre (r=-0.7180, P<0.0001) and C4 titre (r=-0.6891, P<0.0001) were recorded. On the other hand non-significant correlations between urinary adiponectin and other demographic and laboratory parameters were recorded (Table 6).

ROC curve showed that the sensitivity and specificity of serum adiponectin for SLE activity at cut off level of 11.97 µg/ml was 100% & 36.36% respectively. The positive predictive value was 73.08% and the negative predictive value was 100%. The sensitivity and specificity of serum adiponectin for lupus nephritis at cut off level of 11.97 µg/ml was 100% & 26.67% respectively. The positive predictive value was 57.69% and the negative predictive value was 100% (Table 7).

Also, ROC curve showed that the sensitivity and specificity of urinary adiponectin for SLE activity at cut off level of 7.145 µg/g creatinine was 73.68% & 90.91% respectively. The positive predictive value was 93.33% and the negative predictive value was 66.67%. The sensitivity and specificity of urinary adiponectin for lupus nephritis at cut off level of 7.145 µg/g creatinine was 93.33% for the both. The positive & negative predictive value was 93.33% for the both (Table 7).

ROC curve showed that in patients with SLE, the sensitivity and specificity of anti-ds (DNA) for SLE activity at cut off level of 44.5 IU/ml was 100% & 72.73% respectively. The positive predictive value was 86.36% and the negative predictive value was 100%. The sensitivity and specificity of anti-ds (DNA) for lupus nephritis at cut off level of 44.5 IU/ml was 100% & 55.33% respectively. The positive predictive value was 68.18% and the negative predictive value was 100% (Table 7).

Table 1. Clinical manifestations in systemic lupus erythematosus (SLE) patients.

Variables	Number of patients	Percentage %
Fever	15	50
Arthralgia & arthritis	22	73.33
Recurrent mouth ulcer	10	33.33
Photosensitivity	8	26.67
Alopecia	15	50
Malar flush	18	60
Serositis	14	46.67
Hematological manifestations	10	33.33
Seizures	1	3.33
Vasculitis	11	36.67

Table 2. Laboratory data of systemic lupus erythematosus (SLE) patients.

Variables	Range	Mean±SD
ESR 1st hour (mm/hour)	25-120	63.9±28.297
C-reactive protein (CRP) (mg/dl)	0-24	10±5.754
SLEDAI	2-30	13.6±9.19
Renal SLEDAI	0-12	5.33±5.591
Hemoglobin (g/dl)	7.1-12.9	10.41±1.456
White blood cells (WBCs) x 10^9/L	2.5-9.2	5.997±1.848
Platelets x10^9/L	67-305	155.2±62.061
Serum creatinine (mg/dl)	0.7-1.6	1.37±0.1629
Proteinuria (g/24 h)	0.05-2.9	0.73±0.8033
Creatinine clearance (ml/min/1.73 m^2)	43-129	89.20±20.145
Serum C3 (mg/dl)	27-135	80.4±33.508
Serum C4 (mg/dl)	3-45	19.5±13.97
ANA(U/ml) (U/ml)	17-37	23.33±5.435
Anti-ds (DNA) (IU/ml)	10-135	71.20±38.617

Table 3. Comparison between SLE patients & control subjects as regard different variables.

Variables	SLE patients (No = 30) Mean±SD (Range)	Control subjects (No=15) Mean±SD (Range)	P-value
Age (years)	21.84±4.909 (15-32)	23.4±4.421 (17-32)	0.2017
BMI(Kg/m^2)	22.44±0.6279 (21-23.4)	22.35±0.714 (20.9-23.7)	0.7726
Serum adiponectin (µg/ml)	16.98±5.356 (10.84-28.08)	7.92±1.629 (5.45-11.21)	<0.0001**
Urinary adiponectin (µg/g creatinine)	7.95±3.938 (3.97-16.89)	2.73±0.3911(2.01-3.05)	<0.0001**

Table 4. Comparison between SLE patients with lupus nephritis (LN) and without LN and Comparison between active SLE and inactive SLE patients as regard different variables.

Variables	SLE with LN (No=15) Mean±SD	SLE without LN (No=15) Mean±SD	P-value	Active SLE (No=19) Mean±SD	Inactive SLE (No=11) Mean±SD	P-value
Age (years)	21.13±4.658	22.47±5.222	0.4548	21.21±4.744	22.82±5.25	0.4009
Disease Duration (years)	1.68±0.7704	1.5±0.6944	0.5742	1.63±0.7922	1.52±0.627	0.8459
BMI (Kg/m^2)	22.28±0.5967	22.6±0.637	0.0813	22.38±0.6079	22.55±0.6773	0.2721
CRP (mg/dl)	10.4±4.222	8.4±5.914	0.1538	10.42±5.607	7.37±3.88	0.1329
ESR 1st hour (mm/hour)	85.53±21.074	42.27±14.548	<0.0001**	81±20.817	34.36±5.182	<0.0001**
Hemoglobin (g/dl)	10.22±1.589	10.59±1.338	0.4425	10.25±1.529	10.68±1.343	0.4384
WBCs x10^9/L	6.38±1.668	5.61±1.995	0.3836	6.52±1.633	5.1±1.926	0.0741
Platelets x10^9/L	137.8±67.577	172.6±52.563	0.0779	169.58±50.588	130.36±74.106	0.0554
Serum creatinine (mg/dl)	1.93±0.1751	1.08±0.1320	0.1626	1.14±0.2006	1.14±0. 06742	0.6190
Proteinuria (g/24 h)	1.38±0.675	0.09±0.01699	<0.0001**	1.11±0.8023	0.084±0.01859	0.0005*
Creatinine clearance (ml/min/1.73 m^2)	74.2±11.546	104.2±15.006	<0.0001**	79.11±14.783	106.64±15.983	**0.0002
Serum C3 (mg/dl)	52.2±16.24	108.6±18.92	<0.0001**	59.47±20.544	116.55±15.076	<0.0001**
Serum C4 (mg/dl)	7.27±2.492	31.73±8.795	<0.0001**	10.21±6.268	35.55±6.933	<0.0001**
ANA(U/ml)	23.87±6.069	22.8±4.837	0.6931	24.74±5.753	20.91±3.986	0.0551
Anti-ds (DNA) (IU/ml)	95.67±19.167	46.73±37.933	0.0013**	93.68±17.468	32.26±33.998	0.0003**
Serum adiponectin (µg/ml)	19.997±5.999	13.97±1.995	0.0235*	19.09±5.600	13.34±1.935	0.0004**
Urinary adiponectin (µg/g creatinine)	10.94±3.4	4.97±1.204	<0.0001**	9.50±4.146	5.28±1.271	0.0004**

Table 5. Serum & urinary adiponectin in patients with inflammatory LN (class III & IV) & non-inflammatory LN (class I & II).

Variables	Inflammatory LN (class III & IV) patients (No=8) Mean±SD	Non-inflammatory LN (class I & II) patients (No=7) Mean±SD	P-value
Serum adiponectin (µg/ml)	23.73±4.821	15.73±4.130	0.0059**
Urinary adiponectin (µg/g creatinine)	13.67±1.796	7.82±1.398	<0.0001**

Table 6. Correlation between serum & urinary adiponectin and different variables among SLE patients.

Variables	Serum adiponectin		Urinary adiponectin	
	r	P- value	r	P- value
Age (years)	- 0.01453	0.9393	0.07834	0.6807
Disease Duration (years)	-0.06667	0.7263	0.2008	0.2873
BMI (Kg/m^2)	-0.1413	0.4564	- 0.1068	0.5744
SLEDAI	0.7282	<0.0001**	0.5940	0.0005**
Renal SLEDAI	0.5176	0.0034**	0.8331	<0.0001**
ESR 1st hour (mm/hour)	0.6889	<0.0001**	0.5915	0.0006**
CRP (mg/dl)	0.1090	0.5664	0.2539	0.1758
Hemoglobin (g/dl)	- 0.03118	0.8701	- 0.1224	0.5194
WBCs $x10^9/L$	0.1285	0.4986	- 0.07895	0.6783
Platelets $x10^9/L$	0.2637	0.1591	0.2804	0.1333
Serum creatinine (mg/dl)	0.05214	0.7843	0.2058	0.2751
Proteinuria (g/24 h)	0.4535	0.0118*	0.7163	<0.0001**
Creatinine clearance (ml/min/1.73 m^2)	- 0.2677	0.1527	- 0.5122	0.0038**
Serum C3 (mg/dl)	- 0.6343	0.0002**	- 0.7180	<0.0001**
Serum C4 (mg/dl)	- 0.7414	0.0004**	- 0.6891	<0.0001**
ANA(U/ml)	0.1121	0.5554	- 0.05762	0.7623
Anti-ds (DNA)	0.6435	<0.0001**	0.4581	0.0109*
LN class	0.5480	0.0344*	0.7749	0.0007**
Urinary adiponectin(µg/g creatinine)	0.4185	0.0214*		

Table 7. Sensitivity, specificity, positive prediction, negative prediction and accuracy of serum & urinary adiponectin as diagnostic of SLE activity and lupus nephritis among the studied SLE patients.

Variable		Serum adiponectin	Urinary adiponectin	Anti-ds (DNA)
Diagnosis of SLE activity	Area under the curve	0.809	0.7799	0.9091
	P-value	0.006**	0.01185*	0.0000236**
	Cut – off level	11.97	7.145	44.5
	Sensitivity	100%	73.68%	100%
	Specificity	36.36%	90.91%	72.73%
	+ve prediction	73.08%	93.33%	86.36%
	-ve prediction	100%	66.67%	100%
Diagnosis of lupus nephritis	Area under the curve	0.742	0.9733	0.8467
	P-value	0.024*	<0.0001**	0.001223**
	Cut – off level	11.97	7.145	44.5
	Sensitivity	100%	93.33%	100%
	Specificity	26.67%	93.33%	53.33%
	+ve prediction	57.69%	93.33%	68.18%
	-ve prediction	100%	93.33%	100%

N.B.: In all tables above * means statistical significant, ** means statistical highly significant

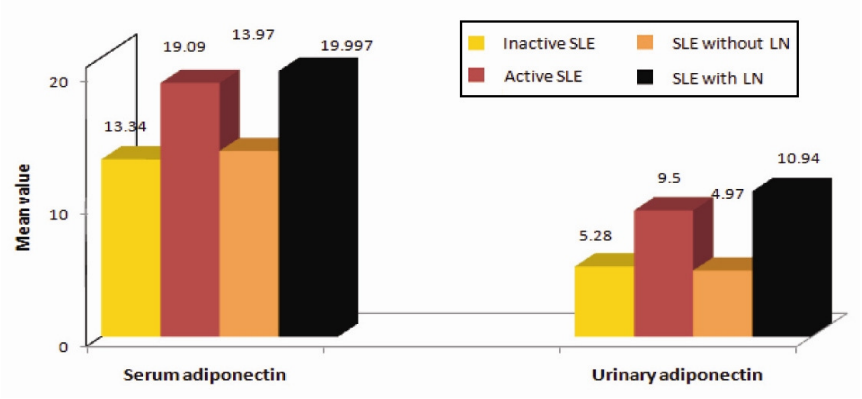

Figure 1. Comparison between SLE with LN & SLE without LN and active SLE & inactive SLE as regard serum & urinary adiponectin.

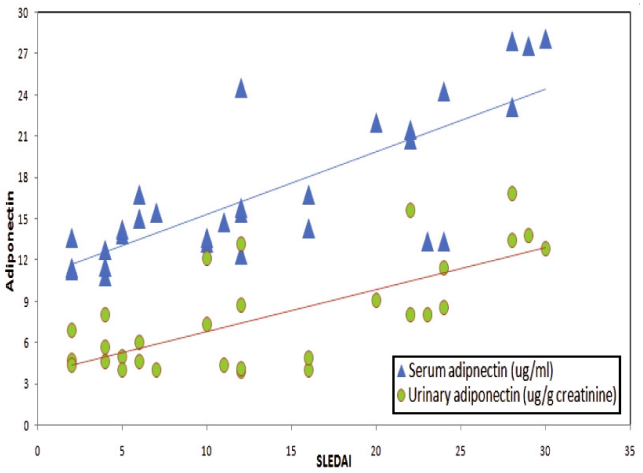

Figure 2. Correlation between serum & urinary adiponectin and SLEDAI.

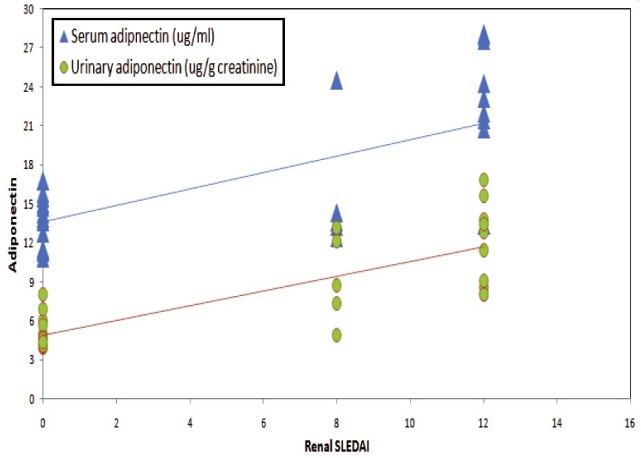

Figure 3. Correlation between serum & urinary adiponectin and renal SLEDAI.

DISCUSSION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by chronic inflammation and the production of autoantibodies directed against numerous antigens. SLE targets multiple organ systems including joints, skin, kidneys, CNS and others organs[1,2]. Renal involvement is common in SLE affecting 50% adult subjects suffering from SLE[3]. Adiponectin is adipocytokine has anti-inflammatory properties[8]. However, its role in SLE & lupus nephritis remains to be clarified, so the aim of this study to assess the level of serum & urinary adiponectin in SLE patients and to detect any relation between serum & urinary adiponectin levels and SLE activity & lupus nephritis.

In this study, a statistically significant higher serum adiponectin level was found in SLE patients when compared with controls. This is in agreement with Sada et al. study in 2006[18], Chung et al. study in 2009[19], De Sanctis et al. study in 2009[20] & Reynolds et al. study in 2010[21], they measured the concentrations of different adipocytokines as adiponectin in patients with SLE and control subjects. They recorded that serum adiponectin was higher in patients with SLE than in controls. They all concluded that adiponectin is involved in the inflammation in SLE. Also Toussirot et al. study in 2010[22] documented that adiponectin levels were higher in patients with systemic autoimmune disease including SLE than in control subjects. In the opposite side Marjon et al. study in 2009[23], Vadacca et al. study in 2009[24] & Vadacca et al. study in 2013[25] found no difference in the adiponectin level between the control and SLE patient group. Tanaka et al. study in 2013[26] found that serum HMW-adiponectin levels were lower in the patients than in the controls at baseline.

Our study showed significantly higher urinary adiponectin level in SLE patients when compared to controls and significantly higher urinary adiponectin level among SLE patients with LN when compared to patients without LN, this is concided with Rovin et al. study in 2005[27], who stated that urine adiponectin levels increased significantly with renal flare, but not non renal SLE flare.

In our study, there was significantly higher serum adiponectin level among SLE patients with LN compared to SLE patients without LN, this is in agreement with Rovin et al. study in 2005[27], who demonstrated that plasma adiponectin levels are increased in patients with renal SLE compared to healthy controls and patients with non renal SLE.

Our result showed higher serum & urinary adiponectin level among inflammatory LN class (III & IV) patients when compared with non-inflammatory LN class (I & II) with statistically highly significant difference. Also Rovin et al. study in 2005[27] demonstrated that, at renal flare the mean plasma adiponectin level in the inflammatory group (class III, IV) was significantly higher than the mean level in the non inflammatory group (class I, Π &V).

In the present study, there was significantly higher serum adiponectin level among active SLE patients compared to inactive patients. Also there was significantly higher urinary adiponectin level among active SLE patients compared to inactive SLE patients

In our SLE patients, serum adiponectin had a highly significant positive correlation with SLEDAI, renal SLEDAI, ESR, proteinuria, anti-ds DNA and LN class while inverse correlation with C3, and C4 were recorded. Zoccali et al. study in 2003[14] stated that 24-hour proteinuria were strongly correlates of plasma adiponectin. Guebre-Egziabher et al. study in 2005[28] demonstrated that adiponectin was negatively correlated with glomerular filtration rate (GFR) & BMI and positive relationship was also found between plasma adiponectin and the urinary albumin/creatinine ratio & no relationship between plasma adiponectin & CRP. Our results disagree with Rovin et al. study in 2005[27], who stated that there was a negative correlation between serum adiponectin & CRP, but no significant correlations between plasma adiponectin and ESR, or proteinuria. Chung et al. study in 2009[19] stated that adiponectin was significantly negatively correlated with BMI and among patients with SLE, adiponectin were not correlate with ESR and SLEDAI but correlate with CRP. Marjon et al. study in 2009[23] stated that there was no correlation of adiponectin concentrations with BMI or SLEDAI score. Toussirot et al. study in 2010[22] stated that ESR and adiponectin were found to be markedly negatively correlated, but no correlation with CRP. However, in our study we did not find a statistical correlation between adiponectin and BMI due to our patients were selected in normal range of BMI.

Our results demonstrated that, urinary adiponectin had a highly significant positive correlation with SLEDAI, renal SLEDAI, ESR, proteinuria, anti-ds DNA and LN class while inverse correlation with creatinine clearance, C3 titre and C4 titre was recorded. Rovin et al. study in 2005[27] stated that, at renal flare, a significant positive correlation between urine adiponectin and urine protein, serum creatinine.

In the present study, serum adiponectin had a significant positive correlation with urinary adiponectin in SLE patients, this is in agreement with Rovin et al. study in 2005[27], who stated that significant correlations between urine and plasma adiponectin.

Some reports surprisingly suggest proinflammatory action of adiponectin[29,30]. It has been

evidenced that the serum concentration of adiponectin is elevated in patients with chronic/autoimmune inflammatory conditions[11]. Although elevated adiponectin levels could be explained by a compensatory response against inflammation, some researchers find this explanation unconvincing and point to the role of adiponectin in NFκB activation[29,30]. This bidirectional, anti- and pro-inflammatory effects of adiponectin may in part result from the changes in the relative proportion of its various isoforms. LMW adiponectin has been shown to block endotoxin-induced secretion of IL-6 and to induce IL-10 production (anti-inflammatory effects), while MMW and HMW adiponectin has been found to stimulate monocyte chemoattractant protein-1(MCP-1) and IL-8 synthesis higher amounts of this isoform may result in pro-inflammatory properties of adiponectin[31]. These findings imply that measurement of adiponectin multimers may adds significant value in assessing role of the adiponectin compared to total adiponectin alone. Certainly, it cannot be excluded that adiponectin production and secretion is regulated in a disease-dependent manner and that adiponectin action depends on a type of inflammatory disorder a patient suffers from.

Conclusion

Serum & urinary adiponectin levels are elevated in SLE patients and strongly associated with lupus activity & LN. Serum adiponectin can't be used as diagnostic test for SLE activity due to very low specificity (36.36%). Urinary adiponectin can be used as diagnostic test for LN with high sensitivity (93.33%) & high specificity (93.33%) and better than anti ds (DNA), but serum adiponectin can't be used as diagnostic test for LN due to very low specificity (26.67%). Serum & urinary adiponectin may consider promising biomarkers for prediction of SLE activity & renal involvement especially urinary adiponectin in lupus nephritis. Further study for measurement of adiponectin multimers in SLE & LN is recommended.

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