Serum and Urinary Interleukin-6 in Assessment of Renal Activity in Egyptian Patients with Systemic Lupus Erythematosus

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ABSTRACT

AIM OF THE WORK: This study investigates whether serum and urinary interleukin-6 (IL-6) represent an early marker of kidney involvement and assesses the difference between them and renal biopsy in lupus nephritis (LN).

PATIENTS AND METHODS: A total of 60 systemic lupus erythematosus (SLE) patients were compared to 20 healthy controls. Urinary and serum IL-6 were measured in both patients and controls. In addition, renal biopsy was done prior or shortly after urine and blood sampling; the results were classified according to the International Society of Nephrology/Renal Pathology Society classification of LN by recording the activity score and chronicity score for each sample.

RESULTS: There was a significant higher level of urinary IL-6 in the SLE patients with biopsy-proven LN than in those without LN and those of the control group. However, no significant difference was reported between the three groups as regards serum IL-6. A strong positive correlation was found between urinary IL-6 and renal disease activity based on the renal SLE disease activity index (SLEDAI) score with no significant correlation regarding the extra renal SLEDAI. Urinary IL-6 was positively correlated with renal biopsy results and with its activity scores but weakly correlated with the chronicity scores.

CONCLUSION: Urinary IL-6 may provide a simple noninvasive potential marker of disease activity of renal involvement in adult patients with SLE.

KEYWORDS: lupus nephritis, SLE, urinary interleukin-6, biopsy in lupus nephritis

Introduction

Renal affection is most common in the systemic lupus erythematosus (SLE) patients, representing 50% of patients. It accounts for significant morbidity and mortality, and 10% of the patients are deteriorated to dialysis or transplantation.[1,2] The 5- and 10-year renal survival rates of lupus nephritis (LN) in the 1990s range between 83%–92% and 74%–84%, respectively.[3] Africans and Hispanics represent the worst prognostic ethnic groups.[4] Despite all new therapies discovered later, its prognosis remains unsatisfactory. Up to 25% of patients still develop end-stage renal failure 10 years after the onset of renal disease.[5]

The oldest parameters such as proteinuria, urine sediments, creatinine clearance, complement levels, and anti-double-stranded DNA (anti-dsDNA) are not sensitive and not specific for the determination of the disease activity of LN and its early relapse. Therefore, new biomarkers are needed to improve the sensitivity and diagnostic accuracy of LN, monitoring of response to therapy, detection of early renal flares, and prognostic stratification.[6]

Interleukin-6 (IL-6) is a pleiotropic cytokine with a wide range of biological activities that plays an important role in immune regulation and inflammation. Among other actions, it induces the terminal differentiation of B lymphocytes into antibody-forming cells and the differentiation of T cells into effector cells. IL-6 also has multiple potent pro-inflammatory effects. An association between IL-6 and lupus was demonstrated in murine models of SLE, and blocking IL-6 improved lupus in all models tested. Data from several studies suggest that IL-6 plays a critical role in the B-cell hyperactivity and immunopathology of human SLE and may have a direct role in mediating tissue damage.[7]

Patients and Methods

Patients. Sixty patients who fulfilled the updated classification criteria of American College of Rheumatology for SLE were enrolled in the present study.[8] These patients were recruited from outpatients or inpatients from the Rheumatology, Internal Medicine, Intensive Care Unit, and Tropical Departments of Minia University Hospital. The exclusion criteria were diabetes mellitus, Malignancies, overlap syndrome (coexistence of lupus with other connective tissue diseases), urinary tract infection (≥100,000 colony-forming units in urine culture), the patients

with renal insufficiency from non-lupus-related causes are excluded and those undergoing hemodialysis or renal transplantation are also excluded. Ethics committee approval was received from Al-Minia University Local Research Ethics for this study. Written informed consent was obtained from patients and controls who participated in this study. The research was conducted in accordance with the principles of the Declaration of Helsinki.

Controls. Patients with lupus were matched to control subjects (group I) on the basis of age and sex status. The control group included 20 persons who were recruited from the secretarial and support staff at the Minia University Hospital, as well as through friends of patients.

Methods. Each SLE patient underwent a complete history taking and physical examination according to a standard protocol sheet. The activity of the disease was assessed by means of the SLE disease activity index (SLEDAI), which covers the symptoms present at the time of the visit or in the preceding 10 days and includes 16 clinical manifestations and 8 laboratory parameters (possible range, 0–105). Higher scores indicate more active SLE.[9]

The renal involvement was assessed with the renal SLE-DAI that consists of four kidney-related parameters of the SLEDAI: hematoria, pyuria, proteinuria, and renal casts. Each item in the renal SLEDAI is assigned 4 points; thus, scores for the renal SLEDAI range from 8 to a maximum of 16. The assessment of disability in the SLE patients was done using the Arabic version of the health assessment questionnaire (HAQ) – disability index.[10]

All patients were subjected to routine Laboratory investigations that include simple urine analysis, complete blood picture (CBC), First hour of erythrocyte sedimentation rate ESR (Westergren method), C-reactive protein, Fasting blood sugar, done on Dimension ES chemical auto-analyzer, Renal function tests which include blood urea and serum creatinine, done on Dimension chemical auto-analyzer, blood sugar, and simple urine analysis.

Special laboratory investigations. Urinary and serum interleukin-6 were measured in both patients and control using the quantitative sandwich enzyme immunoassay technique (ELISA), Anti-ds DNA (by ELISA) ANA (antinuclear antibody by immuno-fluorescence technique), C3 and C4 (complement by diffuplate), and protein in 24 hour urine collection. In addition, all patients were subjected to renal biopsy prior or shortly after urine and blood sampling, and the results were classified according to the International Society of Nephrology/Renal Pathology Society classification of LN,[11] with recording of the activity score and chronicity score for each sample. The SLE patients (group II) were further divided into patients with renal involvement labeled as group IIA and patients without renal involvement labeled as group IIB according to the biopsy result.

Data were analyzed by the Statistical Package for the Social Sciences (Version 18.0 under Windows).[12] Two-tailed tests were used throughout, and statistical significance was set

at conventional 0.05 levels. Descriptive statistics were carried out: the ranges, means, and standard deviations were calculated for interval and ordinal variables and the frequencies and percentages for categorical variables. Group comparisons were done by several procedures, depending on the type of variable.

- Student's *t*-test: The *t*-test was used to compare the difference between the means of two groups in terms of interval and ordinal variables.
- The chi-squared (χ^2) test: The χ^2 test is a nonparametric measure of the statistical independence of the categories of the two variables measured on the nominal or dichotomous scale. The χ^2 test was used to test the significance of the difference between the two groups in categorical variables (eg, sex). receiver operating characteristic (ROC) curve, used for analysis of urinary interleukin-6 levels in patients with LN proven by biopsy (the current gold standard) and patients without renal involvement.

Results

Demographics and treatments. The demographic characteristics of patients are shown in Table 1. The patients' mean age was 27.5 ± 8.2 years (ranging from 19 to 45 years). The mean age at the onset was 24 ± 10 years (ranging from 19 to 35 years). The mean disease duration was 41.7 ± 31 years (ranging from 1 month to 11 years). A strong predominance of female patients was found, 57 females (95%) and 3 males (5%). The mean age of group I was 33.4 ± 14.2 years (ranging from 20 to 45 years) with a strong predominance of female patients, 18 females (90%).

The demographic characteristics of the two groups of SLE patients, such as group IIA and group IIB, are shown in Table 2 with no significant differences in age, age at onset, or duration of the disease between the two groups.

Table 1. Demographic data of SLE patients and controls.

DEMOGRAPHIC DATA	GROUP II (n = 60)		GROUP I (n = 20)	
	RANGE	MEAN ± SD	RANGE	MEAN ± SD
Age (years)	19–45	27.5 ± 8.2	20–45	33.4 ± 14.2
Age at onset (years)	19–35	24 ± 10		
Duration of disease (months)	1–132	41.7 ± 31		

Table 2. Demographic data of SLE patients: group IIA and group IIB.

DEMOGRAPHIC DATA	GROUP IIA (n = 30)		GROUP IIB (n = 30)		P
	RANGE	MEAN ± SD	RANGE	MEAN ± SD	
Age (years)	19–45	27.1 ± 8.2	21–44	28 ± 10.4	0.846
Age at onset (years)	19–45	24.1 ± 11.3	19–42	24 ± 9	0.931
Duration of disease (months)	6–96	36.3 ± 23.6	1–132	48.1 ± 36.3	0.192

Table 3 shows significant differences between group IIA and group IIB in some clinical features, including fever ($P < 0.025$), malar rash ($P < 0.007$), and alopecia ($P < 0.003$), with higher significant differences in group IIA than in group IIB.

Table 4 shows significant differences regarding total SLEDAI ($P < 0.000$), renal SLEDAI ($P < 0.000$), and HAQ-disability ($P < 0.000$), which were higher in group IIA than in group IIB.

Tables 5 and 6 summarize the comparison of the laboratory parameters and the findings of urine analysis between group IIA and group IIB.

By comparing the positivity of immunological markers in group IIA and group IIB, there was significant difference between the two groups as regards anti-dsDNA ($P < 0.036$), C3 consumption ($P < 0.041$), and C4 consumption ($P < 0.001$; Table 7).

The drugs used by group II were nonsteroidal anti-inflammatory drugs in 6 patients (10%), corticosteroids in 44 patients (73.3%), cyclophosphamide in 17 patients (28.3%), antimalarial drugs in 45 patients (75%), and azathioprine in 23 patients (38.3%). The use of corticosteroids and cyclophosphamide was significantly higher in group IIA than in group IIB ($P < 0.003$ and $P < 0.000$, respectively).

Renal biopsy. The renal biopsy results of group II were as follows: Class I (minimal mesangial LN) was present in 5 patients

Table 3. Comparison of clinical manifestations in SLE patients: group IIA and group IIB.

CLINICAL MANIFESTATIONS OF SLE	GROUP IIA (n = 30)		GROUP IIB (n = 30)		X^2	P
	NO.	%	NO.	%		
Arthralgia	10	33.3%	22	73.3%	6.465	0.25
Arthritis	6	20%	15	33.3%	1.129	0.480
Malar rash	21	70%	17	56.7%	12.160	0.007**
Photosensitivity	20	66.6%	13	46.4%	0.000	1.000
Alopecia	22	73.3%	14	45%	13.891	0.003**
Oral ulcers	18	60%	9	30%	3.636	0.162
Fever	18	60%	8	26.7%	5.013	0.025*
Reynaud's phenomenon	14	46.4%	10	33.3%	0.417	0.748
Myalgia	14	46.4%	12	40%	0.102	1.000
Cardiac affection	18	60%	12	40%	1.600	0.343
Pulmonary affection	14	46.4%	10	33.3%	0.417	0.748
Psychotic affection	5	16.7%	5	16.7%	0.000	1.000
G.I.T affection	10	33.3%	12	40%	0.000	1.000
Headache	23	76.7%	24	80%	0.444	0.801
Seizures	6	20%	3	10%	2.118	0.347
Lymphadenopathy	3	10%	0	0%	2.105	0.487

Note: *Significant, **moderate significant.
Abbreviation: GIT, gastrointestinal tract.

Table 4. Comparison of disease activity, severity, and disability in group IIA and group IIB.

DEMOGRAPHIC DATA	GROUP IIA (n = 30)		GROUP IIB (n = 30)		P
	RANGE	MEAN ± SD	RANGE	MEAN ± SD	
Total SLEDAI	17–56	33.1 ± 11.4	2–41	15 ± 8.9	0.000***
Renal SLEDAI	8–16	12 ± 3.7	0	0	0.000***
Extrarenal SLEDAI	5–45	21.1 ± 11.5	2–41	15 ± 8.9	0.067
HAQ- disability	0–3	1.5 ± 1.03	0–2	0.34 ± 0.67	0.000***

Notes: *Significant, **moderately significant, ***highly significant.
Abbreviations: SLEDAI, systemic lupus erythematosus disease activity index; HAQ, health assessment questionnaire.

Table 5. Laboratory findings in group IIA and group IIB.

ITEM	GROUP IIA (n = 30)		GROUP IIB (n = 30)		P
	RANGE	MEAN ± SD	RANGE	MEAN ± SD	
Hb (gm/dl)	6.4–14.5	9.9 ± 1.7	6.9–16	11.3 ± 2.2	0.029*
WBCs/mm^3	2500–27000	6615 ± 5667.1	2500–139000	5820 ± 2689	0.574
Platelets/mm^3	88000–405000	244750 ± 99414.5	54000–400000	261950 ± 85327	0.561
1st hour ESR (mm)	10–125	60 ± 38.3	7–130	40.2 ± 38	0.107
Serum urea (mg%)	12–153	47 ± 33	12–73	26.2 ± 17	0.017*
Serum creatinine mg%	0.55–2.6	1.1 ± 0.51	0.53–1	0.7 ± 0.1	0.039*
24 h urinary protein g	0.5–13.5	2.4 + 3.3	0.1–0.35	0.24 ± 0.08	0.001**
C3 mg%	23–41	32.7 ± 9	111–120	118 ± 8.9	0.001**
C4 mg%	3.5–6.5	5.3 ± 1.3	17–22	19.7 ± 2.3	0.01*

Notes: *Significant, **moderate significant.
Abbreviations: Hb, hemoglobin; WBC, white blood cell; ESR, erythrocyte sedimentation rate; C3, complement 3; C4, complement 4.

Table 6. Simple urine analysis data in the SLE patients of group IIA.

ITEM	GROUP IIA (n = 30)	
	FREQUENCY	%
Albuminuria Absent	3	10%
+	9	30%
++	15	50%
+++	3	10%
Hematuria	18	60%
Pyuria	24	80%
Casts Absent	9	30%
Granular	15	50%
Hyaline and granular	3	10%
Hyaline	3	10%
Proteinuria (gm/24 hours)	Range	Mean ± SD
	0.5–13.5	2.4 ± 3.3

Table 7. Immunologic markers in the SLE patients: group IIA and group IIB.

ITEM	GROUP IIA (n = 30)		GROUP IIB (n = 30)		X^2	P
	NO.	%	NO.	%		
Anti –ds DNA (IU/ml)	24	80%	15	50%	6.627	0.036*
C3 (mg%)	24	80%	12	40%	2.849	0.041*
C4 (mg%)	27	90%	12	40%	10.989	0.001**

Notes: *Significant, **moderately significant.
Abbreviations: Anti-dsDNA, anti-double-stranded DNA; C3, complement 3; C4, complement 4.

(8.3%), Class II (mesangial proliferative LN) was present in 8 patients (13.3%), Class III (focal proliferative LN) was present in 3 patients (5%), Class IV (diffuse proliferative LN) was present in 12 patients (20%), Class V (membranous LN) was present in 1 patient (1.7%), and Class VI (advanced sclerotic LN) was present in 1 patient (1.7%). The mean value of activity score

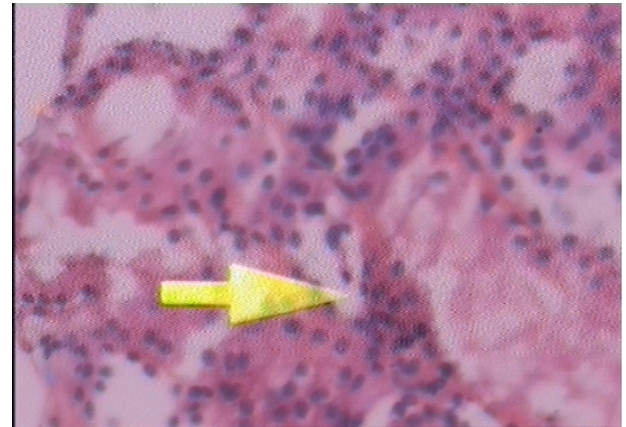**Figure 1.** Class I – minimal mesangial lupus nephritis in our patient.

Figure 2. Class II – Mesangial proliferative lupus nephritis in our patient.

Figure 3. Class III – Focal global glomerular lupus nephritis in our patient.
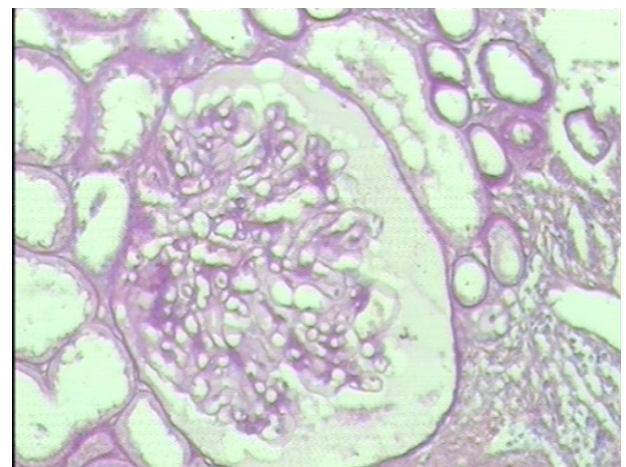

Figure 4. Class IV – Diffuse global glomerulonephritis with hypertensive vascular changes in our patient.

was 6.8 ± 4.6 (ranging from 0 to 15), and the mean value of chronicity score was 2.4 ± 2 (ranging from 0 to 6) (Figs. 1–6).

A strong significant correlation was found between the renal biopsy results and the parameters of disease activity index (SLEDAI), renal SLEDAI ($P < 0.000$) and total
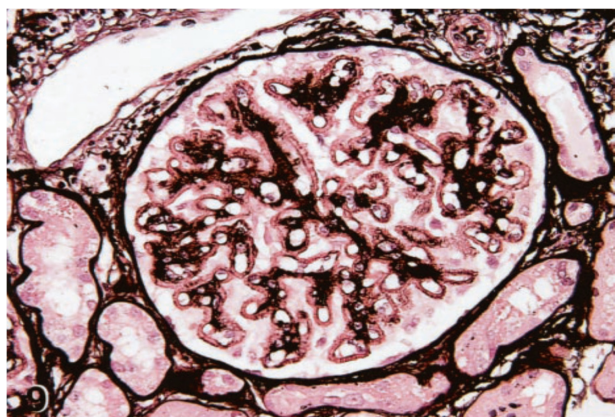
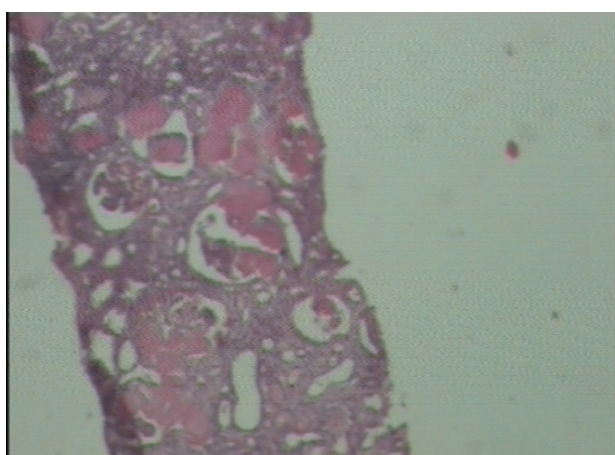**Figure 5.** Class V – Membranous glomerulonephritis in our patient.

Figure 6. Class V1 advanced sclerosis lupus nephritis in our patient.

SLEDAI ($P < 0.00$), with no significant correlation regarding the extra renal SLEDAI.

A positive correlation was found between the biopsy-proven LN, hemoglobin (Hb; $P > 0.029$), serum urea ($P > 0.017$), serum creatinine ($P > 0.004$), anti-dsDNA ($P > 0.003$), C3 consumption ($P > 0.027$), and C4 consumption ($P > 0.016$). No significant correlation

was found between biopsy-proven LN and other clinical manifestations.

Relationship of urinary IL-6 to patient outcomes and disease features. No significant correlation was found between urinary IL-6 and demographic data of group IIA patients as regards age, age at onset, sex, and duration of the disease. There was also no significant correlation between the mean IL-6 and the clinical manifestations of SLE in group IIA patients.

There was no significant correlation between the mean of urinary IL-6 and some laboratory results, such as anti-dsDNA, Hb, white blood cells, platelets, first-hour ESR, serum urea, and serum creatinine. However, there was significant correlation between the mean of urinary IL-6 and some laboratory results as regards proteinuria ($r = 0.83$, $P < 0.02$), C3 consumption ($r = -0.38$, $P = 0.01$), and C4 consumption ($r = -0.44$, $P = 0.01$) in the SLE patients of group IIA. In addition, a strong correlation was found between urinary IL-6 and the doses of corticosteroids and cyclophosphamide taken by group II patients ($P < 0.002$ and $P < 0.003$, respectively).

Our results showed a significant higher level of urinary IL-6 in group IIA than in group IIB and group I. Although no significant difference was reported between the three groups (groups I, IIA, and IIB) as regards serum IL-6 (Table 8), there was an increase in the mean of serum IL-6 in the SLE patients.

Figure 7 shows a positive correlation between the mean IL-6 and renal SLEDAI ($P < 0.000$) and total SLEDAI ($P < 0.029$) but no significant correlation between the mean IL-6 and parameters of extrarenal SLEDAI.

A strong significant correlation was found between the level of urinary IL-6 and the renal biopsy ($P > 0.000$) and the activity score ($P > 0.000$), whereas a weak significant correlation was found between the level of urinary IL-6 and the chronicity score ($P > 0.034$; Fig. 8).

A significant difference in regard to urinary IL-6 was found between Class I LN and Class II LN ($P < 0.019$), while no significant difference was found between Class II LN and Class III LN; however, the mean value of urinary IL-6 was higher in Class III (67 ± 2.5). There was also no significant difference between Class III LN (67 ± 2.5) and Class IV LN

Table 8. Comparisons of urinary and serum interleukin-6 between the different groups.

ITEM	URINARY INTERLEUKIN-6 PG/ML		P	SERUM INTERLEUKIN-6 PG/ML		P
	RANGE	MEAN ± SD		RANGE	MEAN ± SD	
Group I (n = 20)	3.5–8	5.6 ± 1.4		3–8	5.7 ± 1.2	
Group II (n = 60)	5–85	45.2 ± 22.3	0.000***	5–20	15.1 ± 5.9	0.54
Group I (n = 20)	3.5–8	5.6 ± 1.4		3–8	5.7 ± 1.2	
Group IIB (n = 30)	5–13	9.7 ± 1.8	0.1	5–18	11.9 ± 7.4	0.98
Group I (n = 20)	3.5–8	5.6 ± 1.4		3–8	5.7 ± 1.2	
Group IIA (n = 30)	23–85	75.7 ± 9.7	0.000***	16–20	17.3 ± 2.3	0.29
Group IIA (n = 30)	23–85	75.7 ± 9.7		16–20	17.3 ± 2.3	
Group IIB (n = 30)	5–13	9.7 ± 1.8	0.000***	5–18	11.9 ± 7.4	0.22

Note: ***highly significant.
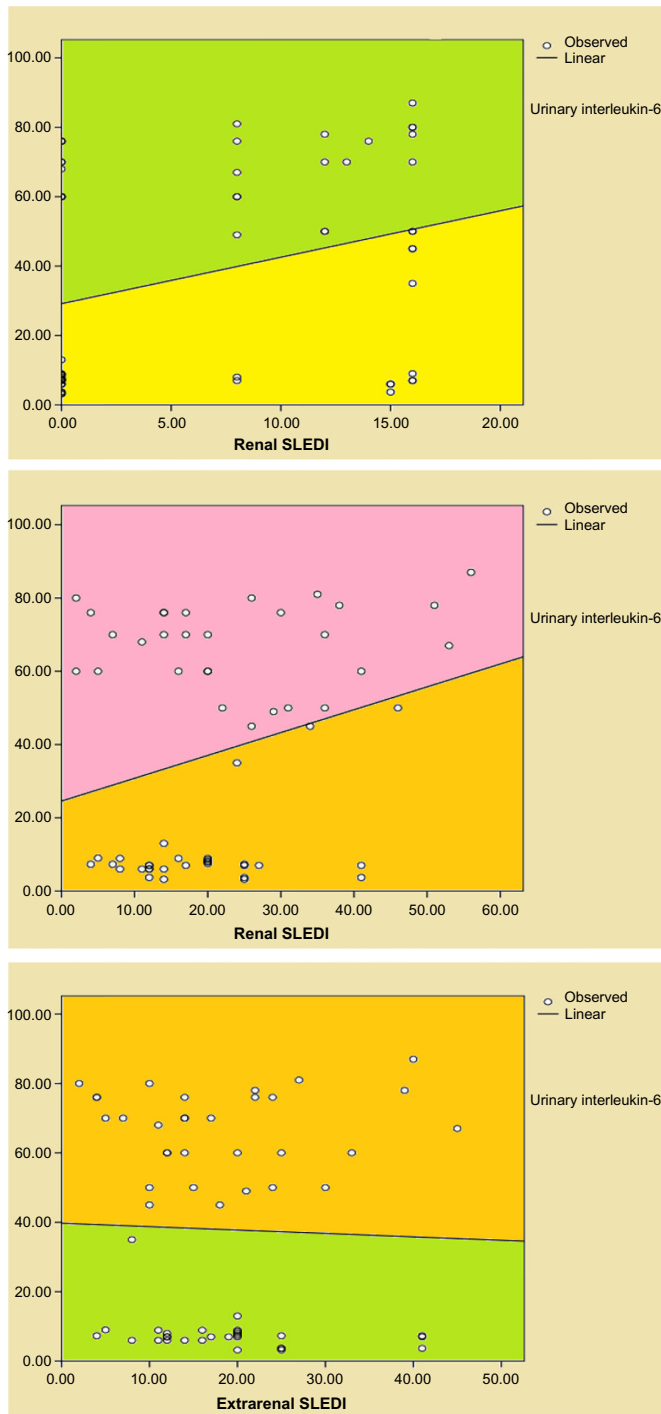
Figure 7. Correlation between IL-6 and renal, total, and extrarenal SLEDAI.

Figure 8. Correlation between urinary IL-6 and renal biopsy, activity score, and chronicity score.

(87.8 ± 3.4); however, the mean value of urinary IL-6 was higher in Class IV (Fig. 9).

A significant higher difference regarding urinary IL-6 was found in group II patients who received corticosteroids and cyclophosphamide than in those who did not use these medications ($P < 0.004$ and $P < 0.005$, respectively).

To quantify the diagnostic utility of urinary IL-6 by ELISA in adult patients with SLE, we constructed an ROC curve. Using a cutoff value of 58.5 pg/mL, urinary IL-6 had a
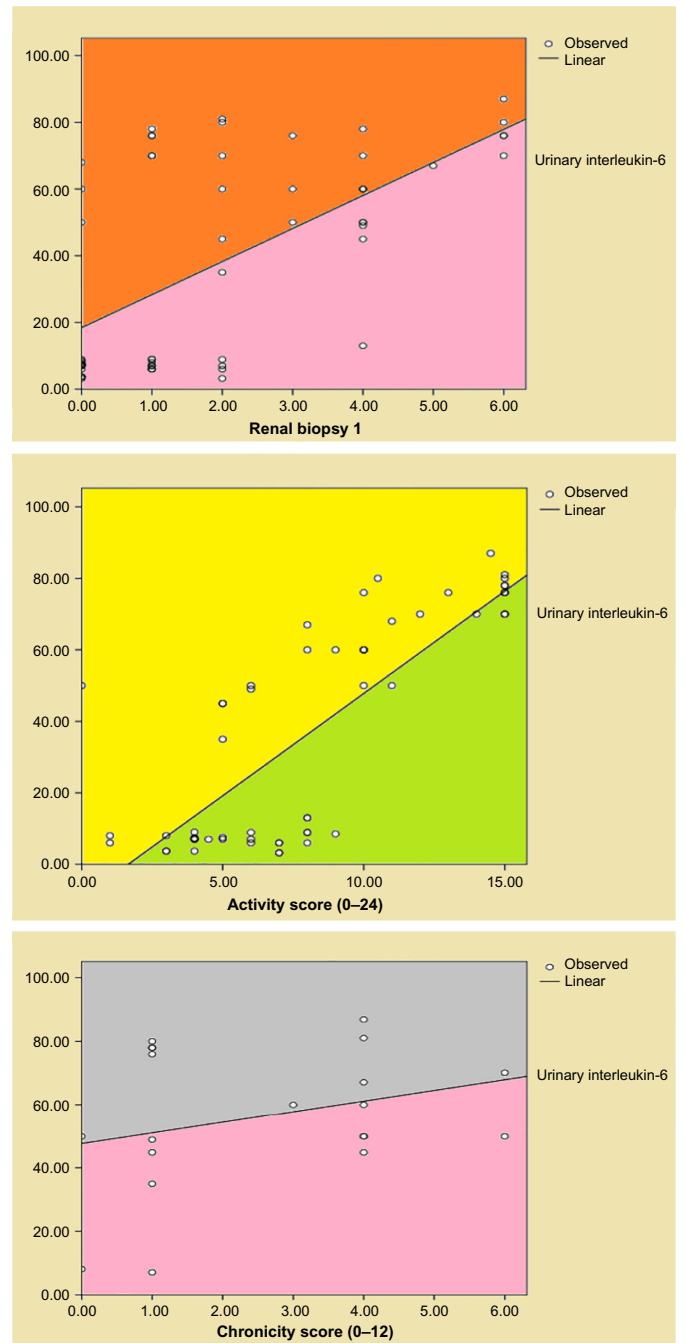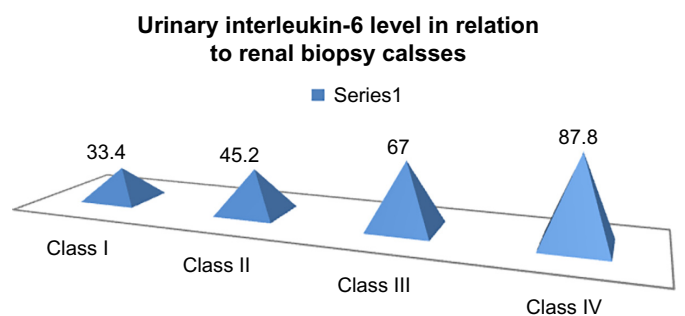

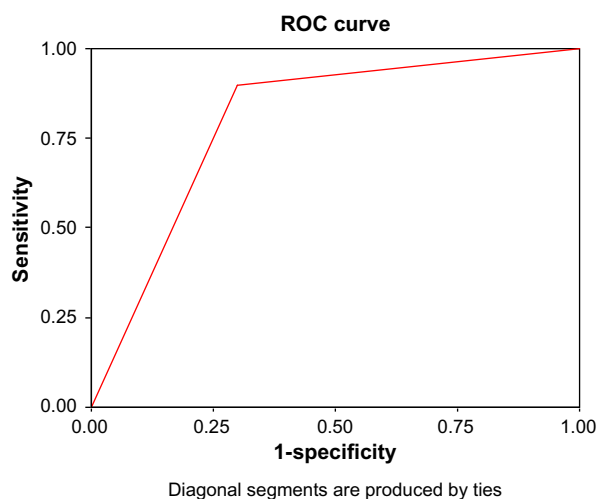**Figure 9.** Urinary IL-6 in relation to renal biopsy classes.

Figure 10. Presentation of sensitivity and specificity of urinary IL-6.

sensitivity of 0.5 and a specificity of 1.0 for identifying the SLE patients with LN. At a cutoff value of 76.5 pg/mL, urinary IL-6 had a sensitivity of 0.6 and specificity of 1.0, and at a cut-off value of 84.5 pg/mL, urinary IL-6 had a sensitivity of 1 and a specificity of 1.0. The corresponding ROC curve is shown in Figure 10. The area under the ROC curve was 0.850.

Discussion

Our data indicate that urinary IL-6 excretion is closely related to renal disease outcomes in the SLE patients rather than to disease activity and damage in extrarenal organ systems, supporting the notion that urinary IL-6 could be a new renal biomarker for the detection of active renal affection in the SLE patients. The data presented suggest that urinary IL-6 is superior to any other renal biomarker assessed in this study for detecting biopsy-proven nephritis in the SLE patients.

In this present study, the level of urinary IL-6 is increased in group II than that of the controls, and this significant difference was due to the higher level of IL-6 in group IIA. Also, no significant difference was detected between lupus patients without nephritis and the normal control group. This was in accordance with the results of other investigators.[13–16]

Moreover, our results reported that urinary IL-6 had highly statistically significant correlation with the renal SLE-DAI. This strongly indicates that the relation of urinary IL-6 with active lupus was dependent on its renal parameters (the renal SLEDAI).[13]

These findings are consistent with the findings of Peterson et al.[13] They asked if levels of serum or urine IL-6 could serve as indicators of lupus disease activity. In all, 16 of 50 SLE patients in whom urine IL-6 was measured exhibited elevated urine IL-6 levels, compared with 1 of 17 controls ($P \leq 0.05$). The levels of urine IL-6 correlated with overall disease activity and with the presence of active urinary sediment. Their results indicate that urine IL-6 may be a marker of active nephritis. In their study, although patients did not

undergo renal biopsy, renal activity was detected by clinical and laboratory data. As we have reported in our study, the more active the renal disease, the higher the levels of urinary IL-6, suggesting that IL-6 may be a biomarker of the presence of active nephritis.

We could not report any relation between the levels of IL-6 and anti-dsDNA antibodies in our patients. However, these laboratory parameters were considered as the indicators of renal activity in clinical practice,[17] and the relation between these laboratory parameters and disease risk is imperfect.[18]

The lack of correlation between the level of urinary IL-6 and serum anti-dsDNA antibodies is surprising for us. This may confirm a possible explanation resulted from the lack of sensitivity of the anti-dsDNA for the specific determination of nephritogenic anti-dsDNA antibodies (that are produced locally in the tissues of kidney) that cause renal disease and upregulate IL-6 expression in the kidneys, and hence, it is measured in urinary excretion while serum anti-dsDNA antibodies represent the summation of locally formed antibodies in the renal tissue which does not measured in serum and the systemic form which measured by serum ELISA.

The role of complement in the pathogenesis of LN has been well described.[19] In our study, urinary IL-6 was correlated with complement consumption, 24-hour protein in urine; these was in agreement with other study.[20]

A strong statistically significant relation was reported regarding the renal biopsy results and SLE renal activity index (the renal SLEDI). In addition, a strong correlation was reported regarding the level of urinary IL-6 and renal biopsy results and score of activity ($P < 0.000$) and a significant but weak correlation was reported regarding the level of urinary IL-6 and the chronicity score. These results are in accordance with other results.[13,14] These results support the relation between the value of urinary IL-6 and the activity of renal affection in the SLE patients with LN.

Moreover, we noticed that a significant difference was found regarding the mean value of IL-6 in different classes of LN, indicating that IL-6 can be used as a good indicator of class of renal nephritis.

In our study, we noticed that the SLE patients taking medications mainly for the treatment of SLE nephritis had increased levels of urinary IL-6 than others. The statistical significance of this was most pronounced in patients who were managed by cyclophosphamide, which supports the possibility that IL-6 is released by the renal tubular epithelium in response to large amounts of filtered protein due to a glomerular capillary leak because alkylating agents are known to cause uroepithelial injury. This may also be attributed to that cyclophosphamide was taken only by the SLE patients with active LN who already have significantly higher levels of urinary IL-6.

Considering corticosteroids, a significant difference was found between SLE patients taking corticosteroids and those who did not take corticosteroids. Also, there was a relation

between the activity of LN and its dose. Whether the treatment by steroid can increase IL-6 production has not been reported. In our patients, severe and more active renal disease was managed by higher doses of steroids, and they had higher levels of IL-6 in the urine.

These results are augmenting the need for further researches considering urinary IL-6 in relation to medications.

The serum concentrations of IL-6 showed no significant relation between group II patients and controls. Also, no statistically significant difference was detected in the levels of IL-6 when comparing patients with LN to those without LN. In addition, the concentration of IL-6 in the serum was not associated with that in the urine of group II patients. These results are in accordance with the results of other studies,[13,14] indicating that the presence of IL-6 in the urine of LN patients is not correlated with the systemic (nonrenal) disease activity and is independent of its serum level; therefore, urinary IL-6 is mostly a consequence of local secretion by the nephritic kidney.

Many urinary parameters have been detected as biomarkers of LN, but none has yet been validated nor has been incorporated into routine practice.[21] If the production of IL-6 is a physiologic response to injury or has a pathogenic or protective role in renal affection is still unknown. An ideal biomarker should detect a clinically relevant process, even if it only measures a physiologic event that has minimal influence on the pathogenesis of lupus.[21]

Our conclusion was that the renal biopsy is an essential tool for monitoring the renal involvement concerning the extent of the lesion as regards classes and degree of both activity and chronicity indices. Despite renal biopsy benefits, it is an invasive and risky procedure with the possibility of insufficient tissue obtained. Urinary IL-6 may provide a simple noninvasive potential marker of disease activity of renal involvement in patients with SLE.

Author Contributions

Collection of patients and taking history: RRE, AL. Analyzed the data: RRE. Wrote the first draft of the manuscript: RRE. Revised the paper: AL. Histopathology: HT. Laboratory work: EAN. Contributed to the writing of the manuscript: RRE, AL. All authors reviewed and approved of the final manuscript.

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