Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 6, 2021, Pages. 6811 - 6822
Received 25 April 2021; Accepted 08 May 2021.

Urinary Angiostatin; A New Biomarker for Early Detection of Lupus Nephritis

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multi- organ involvement, among which kidney is one of the most commonly affected organs.
Objective: The aim of the present study is to evaluate urinary Angiostatin as a new biomarker for early detection of lupus nephritis and its possible role in predicting disease activity.
Subjects and Methods: This was a cross-sectional cohort study conducted on 48 systemic lupus SLE patients; to evaluate whether urinary Angiostatin be a new biomarker for early detection of lupus nephritis. This work carried out on patients in the Nephrology and Immunology Unit of Internal medicine department in Kobri EL Kobba Military Hospital.Subjects included in this study were patients with age group 18-65 years old, of both sexes, diagnosed with systemic lupus erythematosus according to the 1997 American College of Rheumatology (ACR) classification criteria. All persons have been submitted to Full history taking, full clinical examination and Laboratory Investigations as CBC, urine analysis, KFTs, ANA, C3, C4and anti DsDNA.
Results: The average age of all patients was (37.3 ± 11.3) years, the average disease duration was (10.46 ± 6.1) years, the average age of onset was (26.25 ± 8.2) years.The average SLEDAI score was (4.4 ± 3.8), and the average SLICC damage index was (1.77 ± 1.34). Regarding gender of the patients, the majority (85.4%) of patients were females; while (14.6%) were males. Regarding renal biopsy data; the mean activity index was (5.06 ± 4.04) and the mean chronicity index was (1.68 ± 1.38).Regarding ISN/RPS class, (18.8%) of patients had class-I nephritis, (47.9%) had class-II nephritis, (16.7%) had class-III nephritis, (14.6%) had class-IV nephritis, and (2.1%) had class-V nephritis.Significant decrease in age and age of onset in active renal group; compared to other groups. Highly significant increase in SLEDAI score in active renal group; compared to other groups. Highly significant increase in ESR and DNA titer, in active renal group; compared to other groups. Significant increase in activity and chronicity index and ISN/RPS class, in active renal group; compared to other groups.SLEDAI score had a highly significant positive correlation with Urinary Angiostatin; with highly significant statistical difference ($p < 0.01$). Activity and chronicity indices had a highly significant positive correlation with Urinary Angiostatin; with highly significant statistical difference ($p < 0.01$ respectively).
Conclusion: The novel urinary biomarker angiostatin differentiates active renal from active non-renal disease in patients with SLE. The urinary level of this biomarker correlated significantly with SLEDAI, renal SLEDAI and urine protein levels

Key words: Systemic lupus erythematosus (SLE), Urinary Angiostatin, Lupus nephritis.

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1.Introduction:

Approximately 35% of adults show signs of lupus nephritis at the time of SLE diagnosis and 50–60% will develop lupus nephritis (LN) during the first 10 years of disease **(1).**

LN remains the major cause of morbidity and mortality in SLE patients, either as a result of renal failure or secondary to the side effect of aggressive immunosuppressive **(2) .**Glomerulonephritis in patients with SLE significantly reduces their quality of life and working ability**(3)**.

Guidelines for LN diagnosis and management depend largely upon renal pathology, which requires renal biopsy**(4).**Although renal biopsy remains the gold standard for the diagnosis and management of LN, it has several disadvantages. Renal biopsy is invasive, with complications such as bleeding and infection. It is also not feasible to perform renal biopsies repeatedly or serially. Last, but not least, renal biopsy reflects only existing pathology, but cannot predict imminent renal flare in LN patients**(5)**.

Conventional biomarkers for LN, including anti- double- stranded DNA antibodies (dsDNA) and complement components 3 and 4 (C3, C4), are not specific in reflecting concurrent renal activity or predicting impending renal flare**(6)**.

Over the past decade, a myriad of novel biomarkers has been studied in LN. Urinary biomarkers are attractive candidates for tracking LN activity as they are directly excreted from the kidneys and readily available for examination. However, to date, no biomarkers have been adequately validated for routine clinical use in patients with LN**(7)**.

Angiostatin is an endogenous angiogenesis inhibitor produced by autoproteolytic cleavage of plasminogen and has been found to inhibit angiogenesis in cancer through the inhibition of endothelial cell migration, proliferation and induction of apoptosis**(8).**

Urinary angiostatin has been shown to be elevated in patients with active SLE, particularly those with diffuse proliferative LN. Urinary angiostatin differentiates patients with active SLE from those with inactive SLE, and correlated significantly with SLE activity and the renal pathology chronicity index **(9).**

A recent proteomic study revealed increased levels of urinary angiostatin in SLE patients especially in patients with class IV LN, with significant correlation with renal SLICC score as well as the renal pathology chronicity index**(10)**.

Studies found that elevated angiostatin expression in the kidney was related to renal capillary density loss and interstitial damage, which resulted in loss of glomerular function. Studies have demonstrated that angiostatin levels were higher in patients with severe tubule-interstitial lesions, and the significant correlation occurred between the biomarker and 24-h urinary protein excretion. The elevated level of angiostatin expression may aggravate tubule-interstitial damage and proteinuria**(11).**

2.Patients and Method:

This was a cross-sectional cohort study conducted on 48 systemic lupus SLE patients; to evaluate whether urinary Angiostatin be a new biomarker for early detection of lupus nephritis. This work carried out on patients in the Nephrology and Immunology Unit of Internal medicine department in Kobri EL Kobba Military Hospital.

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A total of 48 SLE patients, during a period of six months. were enrolled in the study. After taking their consent to participate in this study, the 48 SLE patients were classified according to renal disease activity into 3 independent groups:Group I: Active non-renal group (5 patients), Group II : Active renal group (15 patients), Group III : Inactive group (28 patients). Active non-renal group in our study (Group I), patients had one or more of the following organ systems affected: dermal, immunologic, central nervous system, and vascular.Active renal group in our study (Group II), patients had renal affection ± one or more of the following organ systems affected: hematologic, dermal, and immunologic.SLE patients must meet the SLICC criteria for SLE diagnosis**(12).**

Patients included in the study were patients with age group 18-65 years old, of both sexes, diagnosed with systemic lupus erythematosus according to the 1997 American College of Rheumatology (ACR) classification criteria.
All patients were subjected to detailed history, full clinical examination.

2.1.Disease activity data*:*

Assessment of disease activity by using the SLE activity measures Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) **(13)**.

- The SLE activity index (SLEDAI) consists of 24 variables covering 9 organ systems (including some immunological tests) scored according to weights derived using multiple regression techniques. A final weighted total SLEDAI score is then calculated. This generated a weighted index of 9 organ systems for disease activity in SLE, the SLEDAI, as follows 8 for central nervous system and vascular, 4 for renal and musculoskeletal, 2 for serosal, dermal, immunologic, and 1 for constitutional and hematologic. The maximum theoretical score is 105. Patient is considered to be in active state if scored 4 or more and considered renally active if there was renal involvement in the form of proteinuria, hematuria, urine casts or elevated serum creatinine level **(13)**.
- Assessment of accumulated damage according to the Systemic Lupus International Collaborative Clinics/ American College of Rheumatology Damage Index (SLICC/ACR DI) **(14)**.

Twelve organ systems are assessed by 41 items for damage, which is defined as non-reversible change that is not related to active inflammation and that has occurred since the onset of lupus, ascertained by clinical assessment and present for at least 6 months. If evidence of damage is noted for a particular item, it is given a score of 1. Some items may score 2 points if they occur more than once, so that the maximum possible score is 47. Scores can only increase with time, but scores rarely reach over 12 **(14)**.

2.2. Laboratory Investigations.

(A) Routine investigations in the form of: Complete blood count, Kidney function tests, estimated GFR, Urine analysis, fasting glucose level, 2 hrs. postprandial glucose level, HbA1C, Plasma sodium, potassium, albumin, bilirubin, Anti-Nuclear Antibody level., Anti Double Stranded DNA level, Complement 3 and 4 levels.

(B) Special investigations in the form of:Urinary Angiostatin

Details of urinary angiostatin test:

Western Blot — Urine levels of angiostatin or other plasminogen fragments were detected using Western blot.

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Table (1): SLICC damage index(14).

Item	Score
Ocular (either eye, by clinical assessment)	
Any cataract ever	1
Retinal change *or* optic atrophy	1
Neuropsychiatric	
Cognitive impairment (e.g., memory deficit, difficulty with calculation, poor concentration, difficulty in spoken or written language, impaired performance level) *or* major psychosis	1
Seizures requiring therapy for 6 months	1
Cerebrovascular accident ever (score 2 if >1)	1 (2)
Cranial or peripheral neuropathy (excluding optic)	1
Transverse myelitis	1
Renal	
Estimated or measured glomerular filtration rate <50%	1
Proteinuria ≥3.5 gm/24 hours *or*	1
End-stage renal disease (regardless of dialysis or transplantation)	3
Pulmonary	
Pulmonary hypertension (right ventricular prominence, or loud P2)	1
Pulmonary fibrosis (physical and radiograph)	1
Shrinking lung (radiograph)	1
Pleural fibrosis (radiograph)	1
Pulmonary infarction (radiograph)	1
Cardiovascular	
Angina *or* coronary artery bypass	1
Myocardial infarction ever (score 2 if >1)	1 (2)
Cardiomyopathy (ventricular dysfunction)	1
Valvular disease (diastolic, murmur, or systolic murmur >3/6)	1
Pericarditis for 6 months, *or* pericardiectomy	1
Peripheral vascular	
Claudication for 6 months	1
Minor tissue loss (pulp space)	1
Significant tissue loss ever (e.g., loss of digit or limb) (score 2 if >1 site)	1 (2)
Venous thrombosis with swelling, ulceration, *or* venous stasis	1
Gastrointestinal	
Infarction or resection of bowel below duodenum, spleen, liver, or gall bladder ever, for cause any (score 2 if >1 site)	1 (2)
Mesenteric insufficiency	1
Chronic peritonitis	1
Stricture *or* upper gastrointestinal tract surgery ever	1
Musculoskeletal	
Muscle atrophy or weakness	1
Deforming or erosive arthritis (including reducible deformities, excluding avascular necrosis)	1
Osteoporosis with fracture or vertebral collapse (excluding avascular necrosis)	1
Avascular necrosis (score 2 if >1)	1 (2)
Osteomyelitis	1
Skin	
Scarring chronic alopecia	1
Extensive scarring or panniculum other than scalp and pulp space	1
Skin ulceration (excluding thrombosis) for >6 months	1
Premature gonadal failure	1
Diabetes (regardless of treatment)	1
Malignancy (exclude dysplasia) (score 2 if >1 site)	1 (2)

* Damage (nonreversible change, not related to active inflammation) occurring since onset of lupus, ascertained by clinical assessment and present for at least **6 months** unless otherwise stated. Repeat episodes must occur at least 6 months apart to score 2. The same lesion cannot be scored twice.

2.3. Renal biopsy:

- Biopsies were taken in Pathology unit in Kobri El Kobba military hospital
- ISN/RPS class**(15)**.

Including activity and chronicity indices

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Data entry, processing and statistical analysis was carried out using MedCalc ver. 18.2.1 (MedCalc, Ostend, Belgium). Tests of significance (ANOVA, Chi square tests, Pearson's correlation and ROC Curve analysis) were used. Data were presented and suitable analysis was done according to the type of data (parametric and non-parametric) obtained for each variable. P-values less than 0.05 (5%) was considered to be statistically significant.

3.Results:

The average age of all patients was (37.3 ± 11.3) years, the average disease duration was (10.46 ± 6.1) years, the average age of onset was (26.25 ± 8.2) years. The average SLEDAI score was (4.4 ± 3.8), and the average SLICC damage index was (1.77 ± 1.34) (Table 2)

Regarding renal biopsy data; the mean activity index was (5.06 ± 4.04) and the mean chronicity index was (1.68 ± 1.38).

Regarding ISN/RPS class, (18.8%) of patients had class-I nephritis, (47.9%) had class-II nephritis, (16.7%) had class-III nephritis, (14.6%) had class-IV nephritis, and (2.1%) had class-V nephritis (Table 3).

Comparative study between the 3 groups revealed; highly significant increase in SLEDAI score in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.01$).

Comparative study between the 3 groups revealed non-significant difference as regards sex, disease duration and SLICC damage index ($p > 0.05$) (Table 4).

Comparative study between the 3 groups revealed; highly significant increase in activity and chronicity index and ISN/RPS class, in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.05$ respectively) (Table 5).

Pearson's correlation analysis showed that;SLEDAI score had a highly significant positive correlation with Urinary Angiostatin; with highly significant statistical difference ($p < 0.01$) (Table 6).

Pearson's correlation analysis showed that; age and age of onset had a highly significant negative correlation with Urinary Angiostatin; with highly significant statistical difference ($p < 0.01$ respectively) (Table 6).

Table (2): Basic clinical and disease activity data among 48 SLE patients

Variables		Frequency (%)
Age (years)		37.3 ± 11.3
Disease duration (years)		10.46 ± 6.1
Age of onset (years)		26.25 ± 8.2
SLEDAI score		4.4 ± 3.8
SLICC damage index		1.77 ± 1.34
Gender	Female	41 (85.4%)
	Male	7 (14.6%)

SLEDAI: systemic lupus erythematosus disease activity score. SLICC: SLE International Collaborative Clinic.

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Table (3): Renal biopsy data among 48 SLE patients:

Variables		Frequency (%)
Activity index		5.06 ± 4.04
Chronicity index		1.68 ± 1.38
ISN/RPS class	I	9 (18.8%)
	II	23 (47.9%)
	III	8 (16.7%)
	IV	7 (14.6%)
	V	1 (2%)

ISN/RPS: International Society of Nephrology (ISN)/Renal Pathology Society (RPS) Classification of lupus nephritis (LN).

Table (4): Comparison between the 3 groups as regards basic clinical and disease activity data using ANOVA and Chi square tests:

Variable		Active non-renal (5)	Active renal (15)	Inactive (28)	ANOVA test
		Mean ± SD	Mean ± SD	Mean ± SD	P value
Age (years)		34.6 ± 8.6	30.8 ± 6.7	41.2 ± 12.1	= 0.011*
Disease duration (years)		5.1 ± 2.8	9.5 ± 4.2	11.9 ± 6.8	= 0.052
Age of onset (years)		23.6 ± 4.9	21.3 ± 6.3	29.3 ± 8.3	= 0.005**
SLEDAI score		8 ± 2.4	8.46 ± 2.1	1.6 ± 1.68	< 0.001**
SLICC damage index		1.4 ± 1.1	2.2 ± 1.1	1.57 ± 1.42	= 0.221
	Variable	Active non-renal (5)	Active renal (15)	Inactive (28)	Chi square test P value
Gender	Female	4 (80%)	12 (80%)	25 (89.3%)	= 0.6678
	Male	1 (20%)	3 (20%)	3 (10.7%)	

Table (5): Comparison between the 3 groups as regards renal biopsy data using ANOVA and Chi square tests:

Variable		Active non-renal (5)	Active renal (15)	Inactive (28)	ANOVA test
		Mean ± SD	Mean ± SD	Mean ± SD	P value
Activity index		2 ± 0.7	10.66 ± 1.34	2.6 ± 1.4	< 0.001**
Chronicity index		1 ± 0.7	3.2 ± 1.1	1 ± 0.86	< 0.001**
Variable		Active non-renal (5)	Active renal (15)	Inactive (28)	Chi square test P value
ISN/RPS class	I	1 (20%)	0 (0%)	8 (28.6%)	< 0.001**
	II	4 (80%)	0 (0%)	19 (67.9%)	
	III	0 (0%)	8 (53.3%)	0 (0%)	
	IV	0 (0%)	7 (46.7%)	0 (0%)	
	V	0 (0%)	0 (0%)	1 (3.5%)	

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Table (6): Pearson's correlation analysis for clinical / laboratory / histological Factors associated with Urinary Angiostatin

Associated Factor		Urinary Angiostatin	
		r	P
Clinical	**Age** (years)	-0.4232	=0.0027**
	Disease duration (years)	-0.1586	=0.2818
	Age of onset (years)	-0.4370	=0.0019**
	SLEDAI score	0.6725	<0.0001**
	SLICC damage index	0.2036	=0.1650
Lab	**Hb** (g/dL)	-0.02662	=0.8574
	PLT (10^3/µL)	0.2063	=0.1595
	TLC (10^3/µL)	-0.1850	=0.2082
	ESR (mm/h)	0.4324	=0.0021**
	CRP (mg/dL)	0.2055	=0.1612
	Creat. (mg/dL)	0.08544	=0.5636
	Na (mEq/L)	-0.07051	=0.6339
	K (mEq/L)	0.1666	=0.2576
	Alb. (g/dL)	-0.7186	<0.0001**
	T. Bil. (mg/dL)	-0.1827	=0.2140
	HbA1C (mg/dL)	-0.2053	=0.1616
	Anti-ds DNA titer	0.2657	=0.0680
	C3 (mg/dL)	-0.6843	<0.0001**
	C4 (mg/dL)	-0.6345	<0.0001**
Histological	**ISN/RPS class**	0.7605	<0.0001**
	Activity index	0.7977	<0.0001**
	Chronicity index	0.6413	<0.0001**

r: Pearson's rho (correlation coefficient).

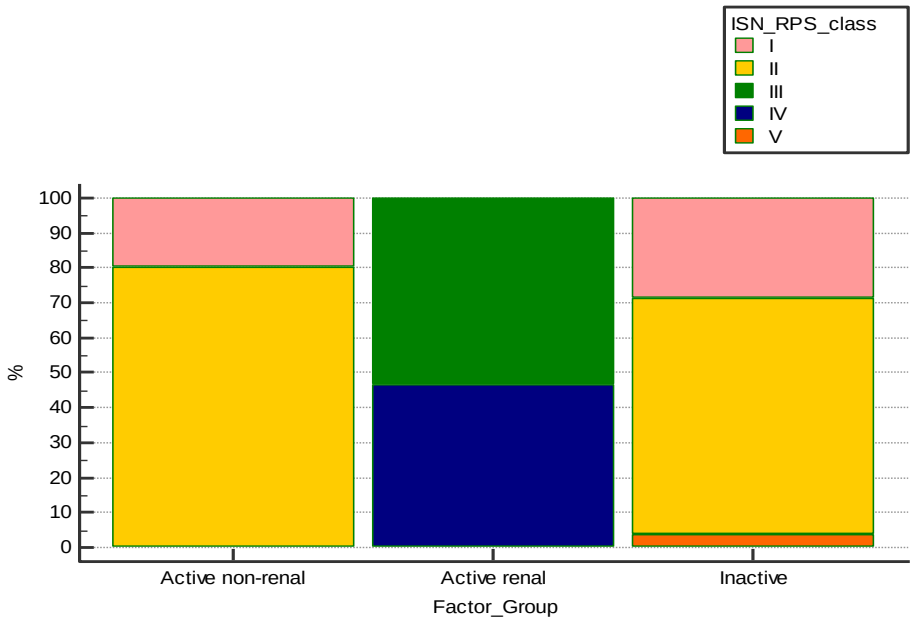

Figure (1): Comparison between the 3 groups as regards ISN/RPS class.

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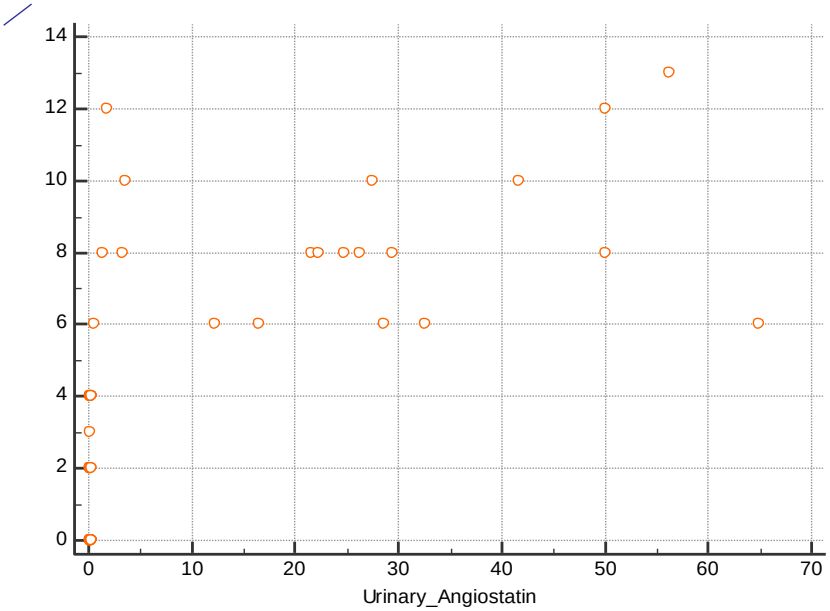

Figure (2): Correlation between Urinary Angiostatin and SLEDAI score

4.Discussion:

Regarding clinical data, we found that; the average age of all patients was (37.3 ± 11.3) years, the average disease duration was (10.46 ± 6.1) years, the average age of onset was (26.25 ± 8.2) years, the average SLEDAI score was (4.4 ± 3.8), and the average SLICC damage index was (1.77 ± 1.34), the majority (85.4%) of patients were females; while (14.6%) were males which came in agreement with ***El-Sayed et al.*****(16)**, ***Pedersen et al.*****(17).**

Pedersen et al. **(17)**, reported that, they performed western blot on human urine samples from healthy controls and SLE patients with and without lupus nephritis. Mean age (range) was 41.5 (21–72) in health group, was 49.5 (30–69) in SLE without LN and was41.7 (20–73) in SLE with LN group. Sex ratio (female: male) was 19:4 in health group, was 24:0 in SLE without LN and was 25:9 in SLE with LN

El-Sayed et al. **(16),** reported that Inactive SLE was reported in 6 (24%) patients with SLEDAI = 0. Twelve (48%) patients had mild SLE activity (SLEDAI= 2– 4 with a median of 2) and 6 (24%) had moderate lupus activity (SLEDAI = 6– 10 with a median of 6). Also reported that SLE patients group: They were 20 (83.3 %) females and 4 (16.7 %) males.

Regarding renal biopsy data; the mean activity index was (5.06 ± 4.04) and the mean chronicity index was (1.68 ± 1.38). ISN/RPS class, (18.8%) of patients had class-I nephritis, (47.9%) had class-II nephritis, (16.7%) had class-III nephritis, (14.6%) had class-IV nephritis, and (2.1%) had class-V nephritis, which came in agreement with ***Brunner et al.*** **(18) ,** who stated that, The GFR was moderately associated ($r = -0.5$; $p < 0.005$) with both histological activity (NIH-AI) and chronicity (NIH-CI), with Disease activity was 7.8 ± 5.2. Most patients had notable proteinuria at baseline, and a majority had an active urinary sediment and ISN/RPS class IV LN. There were no patients with class I or class VI LN. Twelve patients had an NIH-CI score of 0, and three of them also had an NIH-AI score of 0. ISN/RPS class was Class II was 8 (9%), Class III was 16 (18%), Class IV was 35 (40%), and Class V was 29 (33%).

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Comparative study between the 3 groups revealed; highly significant increase in SLEDAI score in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.01$), which came in agreement with ***Li et al.*** **(19)**, which reported that, Proteomic approaches, such as two-dimensional gel electrophoresis, mass spectrometric and/ or immunochemical identification of proteins, surface enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS)and capillary electrophoresis-MS, have been used to screen potential urine biomarkers that are associated with renal damages caused by LN, these revealed that highly significant increase in SLEDAI score in active renal group.

Comparative study between the 3 groups revealed; highly significant increase in ESR and DNA titer, in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.01$ respectively), which came in agreement with ***Yang et al.*** **(20),** who reported that Forty-two patients fulfilling the 1997 revised American College of Rheumatology classification criteria for SLE were recruited. These patients were further divided into SLE-active nephritis (active LN, $n = 24$), SLE-renal (active LN, $n = 24$; and proteinuria alone, >0.5 g/day, $n = 10$), and SLE-non-renal ($n = 8$) groups. ESR 1 hour (mm) was 44 (32) in SLE active group, was (16) 49 in SLE renal group and was (30) (22) in SLE non-renal group.

Comparative study between the 3 groups revealed; highly significant increase in Urinary Angiostatin, in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.01$,which came in agreement with ***Wu et al.*** **(9),** ***Algergawy et al.*** **(21),** ***Mohamed et al.*** **(22)**.

Wu et al. **(9)** reported that, urinary angiostatin was significantly increased in SLE patients compared with healthy controls ($p >0.0001$)**.**

lgergawy et al. **(23)**reported that, SLE patients had elevated urinary angiostatin as compared to controls ($P < 0.001$). Levels of urinary angiostatin were higher in patients with an active LN (lupus nephritis) than those with inactive LN ($P < 0.001$). LN patient's urinary angiostatin correlated with the renal score of the Systemic Lupus Erythematosus Disease Activity Index. Urinary angiostatin levels varied significantly andthere is significant positive correlation ($P <0.05$) levels with the activity and chronicity scores of the examined renal biopsies among the histopathological groups.

Mohamed et al. **(24)** reported that, the urine levels of angiostatin in the 4 groups of subjects studied was significantly higher in patients with active renal disease than active non-renal disease, inactive SLE or healthy controls.

Comparative study between the 3 groups revealed; highly significant increase in activity and chronicity index and ISN/RPS class, in active renal group; compared to other groups; with highly significant statistical difference ($p < 0.05$ respectively) which came in agreement with ***Yang et al.*** **(20)**and ***Hahn et al. 2012.***

Yang et al. **(20)**reported that, data reveal that the SLE-renal group had higher SLE Disease Activity Index (SLEDAI) scores (median, 14; IQR, 10 versus median, 8; IQR, 5; $P = 0.000$) than did the SLE-non-renal group.

Hahn et al.**(4)**reported that,glomerular disease can be classified by current ISN/ RPS classification. In addition, disease can be evaluated for activity and chronicity and for tubular and vascular changes. Finally, biopsies may identify additional or alternative causes of renal disease, such as tubular necrosis related to medications, hypovolemia, or hypotension.

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***Wu et al.* (7)**reported that, Urinary Angiostatin is Able to Discriminate Active SLE from Inactive SLE. After determining that urinary angiostatin is significantly increased in SLE, we next asked whether urinary angiostatin levels reflect disease severity. We further divided the SLE patients into an inactive SLE group (SLEDAI _<2, renal SLEDAI =0), and an active SLE group (SLEDAI >2, renal SLEDAI >0; "lupus nephritis" or "LN"). Within the inactive SLE group, we further distinguished two subgroups: those with past history of nephritis and those without past nephritis. Compared with healthy controls, the urinary angiostatin level was significantly increased among the inactive SLE patients with past nephritis but not in the subgroup without past nephritis (*p* <0.0001). Urinary Angiostatin reflects renal chronicity changes in Lupus nephritis in concurrent biopsy samples. In order to evaluate precisely how well urinary angiostatin can predict particular changes in renal pathology, we collected urine samples from the patients on the same day renal biopsies were performed. We then measured urinary angiostatin levels and compared them with the renal pathology activity index and the renal pathology chronicity index in these paired urine/ biopsies.

***Aljaberi et al.* (23)**reported that urinary angiostatin was able to discriminate between active vs inactive LN patients with good correlation to SLEDAI, renal SLEDAI and SLICC scores.

***Aragón et al.* (24)**reported that angiostatin levels are higher in SLE patients in remission with a previous LN history, in comparison with SLE patients in remission without prior LN**.**

Our result came in disagreement with ***Mok et al.* (25)**who reported that angiostatin was able to discriminate SLE with disease activity and renal involvement vs. SLE patients with active disease but no renal compromise, although there was no correlation with the chronicity indexes in the kidney biopsies. There are two possible reasons for the lack of correlation: Firstly, probably related to the limited sample of patients with different histological classes of LN.Secondly, considerable proportion of patients had mixed histological classes of LN in that study.

5.Conclusion

the novel urinary biomarker angiostatin differentiates active renal from active non-renal disease in patients with SLE. The urinary level of this biomarker correlated significantly with SLEDAI, renal SLEDAI and urine protein levels.

6.Conflict of Interest: No conflict of interest.

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Received 25 April 2021; Accepted 08 May 2021.

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