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ORIGINAL ARTICLE

Role of Urinary sCD25 as a Biomarker in Lupus Nephritis

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Abstract

Background: ***A chronic autoimmune disorder that can impact any organ or tissue, systemic lupus erythematosus (SLE) is a global condition. A disease involves the interaction of hormonal fluctuations, environmental triggers, and genetic predisposition.***

Aim and objectives: ***To determine the relationship between urinary sCD25 and lupus nephritis (LN) activity.***

Subjects and methods: ***Prospective research was done on 60 cases (57 female and three male) and 25 adult persons (20 female and five male) as a control group. This study was done in Al-Azhar University Hospital Asyut's nephrology unit and Elhussin Universal Hospital's nephrology unit, with informed written consent from all participants.***

Results: ***Regarding symptoms, all controls had no chronic disease. Asthma, cardiac diseases, DM, and HTN were observed in 8 (13.33%), 3 (5%), 12 (20%), and 10 (16.67%) cases group, respectively. There was a significant increase in DM and HTN observation in the cases group. All case groups were managed with steroids. Also, in the cases group, 8 (13.33%), 13 (21.67%), and 16 (26.67%) were managed with Azathioprine, Cyclophosphamide, and Hydroxychloroquine, respectively. No medicine was recorded in the control group. There was a significant positive association among WBCs, Urea, Creatinine, ESR 1st h, ESR 2nd h, UP/Creatinine ratio, C3, C4, and CD25.***

Conclusion: ***Urinary CD25 349.5 is a useful noninvasive biomarker for examining renal disease affection in cases with LN since it is strongly associated with various laboratory and clinical markers.***

Keywords: Lupus Nephritis; Urinary sCD25; renal dysfuction

1. Introduction

The autoimmune illness SLE can affect every organ and tissue in the body. Environmental, genetic predisposition and hormonal factors interact with illness .[1]

Haematuria, hypertension, proteinuria, and varying degrees of kidney impairment are all symptoms of glomerulonephritis, a diverse collection of disorders .[2]

Around 50%- 70% of people with SLE also develop LN. Proteinuria, active urine sediment, and a positive kidney biopsy result are the typical criteria for diagnosing LN .[3]

Serum creatinine, proteinuria, and blood urea nitrogen are the most common indicators utilized today for the early diagnosis of chronic kidney disease or acute kidney damage. However, all of them fall short of the ideal and put too much emphasis on treating injuries after they have progressed to a point when treatment is less likely to be helpful .[4]

A renal biopsy is the most reliable method of determining the histological types of LN and the relative levels of activity and chronicity in the glomeruli. Nevertheless, it is invasive and requires repeated biopsies, which makes monitoring LN impracticable .[5]

Autoimmune illness is correlated with elevated sCD25 receptor expression, which may be related to enhanced T-cell and B-cell activation. Cases with LN have been shown to excrete sCD25 in their urine, which may serve as a surrogate measure of T-cell activity in the kidney .[6]

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Urine is an excellent noninvasive tool for studying the immunopathogenesis of LN at the local level. A recent investigation demonstrated that urinary CD25 is a sensitive and specific indicator of renal SLE flare .[6]

The objective of this investigation was to find out the relationship between urinary sCD25 and LN activity.

2. Patients and methods

Our study is an 8-month prospective study conducted on 60 patients (57 female and three male) and 25 (20 female and five male) adult persons as a control group. This study was done in Al-Azhar University Hospital Asyut's nephrology unit and Elhussin Universal Hospital's nephrology unit, with informed written consent from all participants. Group I includes 60 patients (57 female and three male), ages between 25 and 50 years, diagnosed with LN confirmed by renal Biopsy. Group II includes 25 healthy volunteers, matched for age and sex, with the previous group as a control group.

2.1.Inclusion criteria

adult patients >18 years old with established LN by clinical and renal Biopsy will be included.

2.2.Exclusion criteria

young patients <18 years old, pregnant females, patients with incomplete data, and patients with a positive medical history of other chronic diseases or infections.

2.3.Methods

All subjects have been subjected to the following :

Patients with SLE should have a thorough medical history taken, with particular attention paid to their disease activity as determined by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), as well as their age, disease duration, urinary symptoms, SLE manifestations (like rash, cutaneous photosensitivity, joint pain & CNS symptoms like seizures), hypertension symptoms like vomiting, headache, blurred vision, and type of therapy they have been receiving. Comprehensive clinical examination comprising vital signs and anthropometric assessments (weight and height), skin rash distribution, joint discomfort, chest and heart examination, stomach examination, and central nervous system examination. LN statistics: (There is/is not an existence. In a clinical setting. Experiments in a lab. Biopsy of the kidneys). (Serum creatinine and blood urea nitrogen (BUN)) laboratory tests. Evaluation of urine for the ratio of protein to creatinine. Blood count total. The mean time for red blood cells to settle after being in circulation. Direct immunofluorescent assay for anti-DNA (deoxyribonucleic acid) antibodies. Measurement of complement subunits 3 and 4 using radioimmunodiffusion. sCD25 in urine was measured by Enzyme-Linked Immunosorbent Assay (ELISA)).

2.4.Ethical issues

The data will be treated confidentially so that the study does not include any risk to patients. Prior written consent will be obtained for each patient. The study will be presented to the Ethics Committee of Al-Azhar University Hospital in Asyut for approval.

2.5.Statistical analysis

At the end of the study, all data will be collected, tabulated, and statistically analyzed.

3. Results

Table 1. show comparison between patients group and healthy control group regarding to age , sex , body mass index (BMI) and duration of disease .

	CASES GROUP (N = 60)	CONTROL GROUP (N = 25)	P. VALUE
AGE (YEARS)	36.05 ± 7.28	35.72 ± 7.55	0.85099
SEX			
• FEMALE	57 (95%)	20 (80%)	0.03107*
• MALE	3 (5%)	5 (20%)	
BMI	30.03 ± 3.23	26.88 ± 1.2	0.00001*
DURATION OF DISEASE (YEARS)	2.24 ± 0.97	-	-

BMI = body mass index

*Statistically significant at P<0.05.

There was no significant variance among the two groups concerning age.

There is a significant statistical variance among the two groups concerning sex and BMI. Table 1

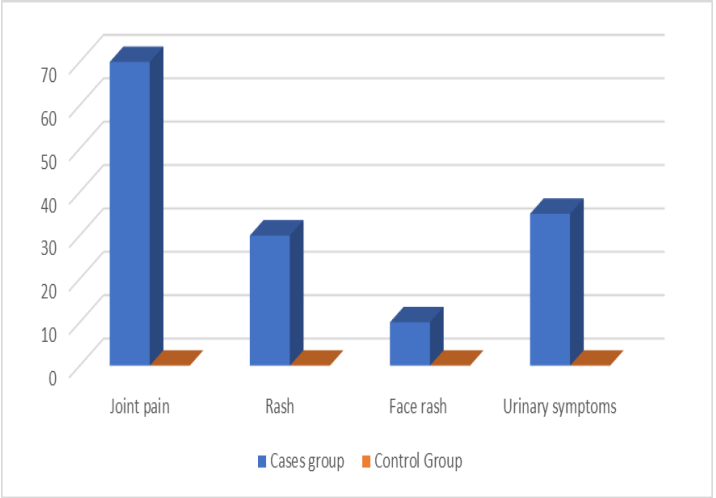

Figure1. Symptoms observed in both groups.

Table 2. Show comparison between patients group and healthy control group regarding to chronic diseases .

	CASES GROUP (N = 60)	CONTROL GROUP (N = 25)	P. VALUE
BRONCHIAL ASTHMA	8 (13.33%)	0	0.05603
CARDIAC INSULT	3 (5%)	0	0.26027
DM	12 (20%)	0	0.01554*
HTN	10 (16.67%)	0	0.02989*

DM= diabetes mellitus
HTN= hypertension

Regarding symptoms, all controls had no chronic disease .Asthma, cardiac diseases ,DM and HTN was observed in 8 (13.33%), 3 (5%), 12 (20%) and 10 (16.67%) of cases group respectively.There was significant increase in DM and HTN observation in cases group. However, although number of asthmatic cases and cases with cardiac diseases were higher in cases group there was no significant variance among cases & control groups. Table 2

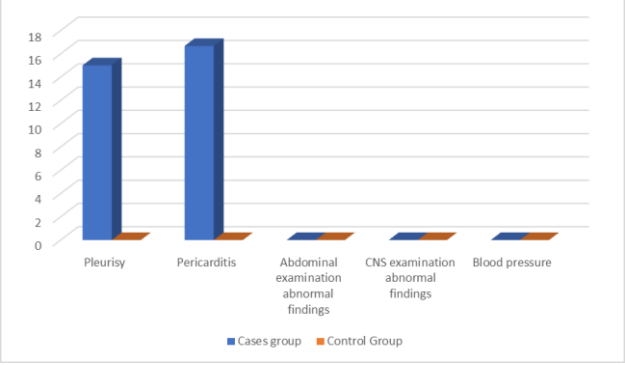

Figure 2. General Examination of subjects in both groups.

Table 3. Show comparison between patients group and healthy control group regarding to general examination.

	CASES GROUP (N = 60)	CONTROL GROUP (N = 25)	P. VALUE
CHEST EXAMINATION			
PLEURISY	9 (15%)	0	0.04103*
HEART EXAMINATION			
PERICARDITIS	10 (16.67%)	0	0.02989*
BLOOD PRESSURE			
- SBP (MMHG)	121.62 ± 15.33	120.56 ± 13.64	0.76586
- DBP (MMHG)	79.65 ± 8.77	79.72 ± 8.34	0.97295
ABDOMINAL EXAMINATION	0	0	-
CNS EXAMINATION	0	0	-

SBP= systolic blood pressure
DBP= diastolic blood pressure

There were no abnormal findings in abdominal or CNS examination. However, pleurisy and pericarditis were significantly elevated in cases group compared with normal group with 9 (15%) cases of pleurisy and 10 (16.67%) cases of pericarditis.There was no significant variance in blood pressure of both groups. Table 3)

Table 4. Show comparison between patients group and healthy control group regarding to treatment.

	CASES GROUP (N = 60)	CONTROL GROUP (N = 25)	P. VALUE
STEROIDS	60 (100%)	0	<0.0001*
AZATHIOPRINE	8 (13.33%)	0	0.05603
CYCLOPHOSPHAMIDE	13 (21.67%)	0	0.01108*
HYDROXYCHLOROQUINE	16 (26.67%)	0	0.00379*

All cases group were managed with steroids. Also in cases group, 8 (13.33%), 13 (21.67%) and 16 (26.67%) were managed with Azathioprine, Cyclophosphamide and Hydroxychloroquine respectively. No medicine was recorded in control group. Table 4

Table 5. Lab Evaluation of subjects in both groups.

	CASES GROUP (N = 60)	CONTROL GROUP (N = 25)	P. VALUE
HEMOGLOBIN (G/DL)	11.57 ± 0.79	11.6 ± 0.75	0.86725
PLT	263.8 ± 46.64	269.76 ± 44.27	0.58745
WBCS	9260.67 ± 904.91	6087.2 ± 1037.16	<0.0001*
UREA (MG/DL)	24.23 ± 2.97	17.72 ± 1.79	<0.0001*
CREATININE (MG/DL)	1.02 ± 0.09	0.82 ± 0.05	<0.0001*
ESR 1ST H	29.77 ± 4.66	15.04 ± 2.17	<0.0001*
ESR 2ND H	38.5 ± 4.76	22.16 ± 1.99	<0.0001*
UP/CREATININE RATIO	3.4 ± 0.52	0.14 ± 0.01	<0.0001*
ANTI-DSDNA	405.58 ± 95.58	-	-
C3 (MG/DL)	34.19 ± 4.47	138.4 ± 6.36	<0.0001*
C4 (GM/L)	0.05 ± 0.02	0.23 ± 0.03	<0.0001*
US CD25	543.35 ± 125.09	377.96 ± 22.6	<0.0001*
SLEDAI SCORE	9.07 ± 3.13	-	-
RENAL SLEDAI	8.95 ± 2.45	-	-

Our study displayed that there were no significant variance among case group and control group regarding Hemoglobin(g/dl) and plt . But ESR ,WBC, Urea (mg/dl) , creatinine (mg/dl) ,UP/CREATININE RATIO , C3 (Mg/dl) , C4(gm/l) and US CD25 were significantly greater in case group than control group. Table 5

Table 6. ROC curve analysis of association between CD25 and Lupus Nephritis.

	CUT OFF VALUE	AUC	SENSITIVITY	SPECIFICITY	ASYMPTOTIC 95% CONFIDENCE INTERVAL		P. VALUE
					Lower Bound	Upper Bound	
CD25	349.5	0.948	98.3%	88%	0.89664	0.99936	<0.0001

With cutoff value 349.5 AUC was 0.948 with significant association between CD25 and LN (P<0.0001). Sensitivity reached 98.3% and specificity reached 88%. Table 6

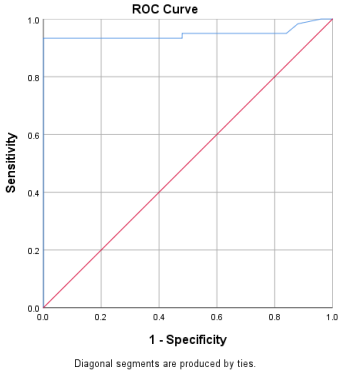

Figure 3. ROC curve analysis of association between CD25 and Lupus Nephritis

4. Discussion

SLE is a chronic autoimmune disease that has the potential to involve every system in the body. Genetic predisposition, environmental factors, and hormonal are interactions in illness .[1]

Fifty percent to seventy percent of those with systemic lupus erythematosus (SLE) develop LN. Proteinuria, active urine sediment, and confirmation by kidney biopsy are the typical diagnostic criteria for LN .[3]

The main results of our study were as follows:

Concerning demographic characteristics, age did not differ significantly between the two groups. The number of females in the Cases group was significantly greater. The BMI of the Cases group was considerably more significant.

On the other hand, Salam et al.[7] enrolled twenty patients with SLE, seven of whom were male and thirteen female. Among the thirty cases, forty percent identified as male and sixty percent as female. Gender and age disparities among groups were not statistically significant. The cases experienced a significant rise in body weight compared with the control group.

In contrast, the participants in the research done by Gaballah et al.[8] were categorized as follows: (i) 25 individuals with SLE & LN (group I); (ii) 25 individuals with SLE and LN who had not received treatment for three months; (iii) 25 individuals with SLE and LN who had not developed the disease; (group III) comprised of 25 individuals who were otherwise healthy. About age and gender, no statistically significant distinctions were observed among the different groups.

The present study showed that all controls were normal regarding symptoms. Joint pain, skin rash, face rash, and urinary symptoms were observed in 42 (70%), 18 (30%), 6 (10%), and 21 (35%) of the cases group, respectively.

Our findings were corroborated by the research of Salam et al.[7], who documented that joint pain is the prevailing initial manifestation in our cases of SLE (85%), with urinary symptoms and skin dermatitis following suit at 50% each. Urinary symptoms were found to be more prevalent in cases with active nephritis of SLE contrasted with those without nephritis. These findings are consistent with those of Cameron[9], who reported that patients with LN initially exhibit urine or renal function abnormalities. However, it is worth noting that up to 60 percent of adults and 80 percent of children may develop overt renal abnormalities in the future.

In contrast, Hassan et al.[10] identified cutaneous manifestations such as hair loss, photosensitivity, and malar dermatitis in 31 (58%) individuals with SLE. Musculoskeletal manifestations observed in 33 individuals (62.3%) comprised arthralgia, arthritis, and myalgia. In addition, thirteen patients (24.5%) exhibited neurological complications involving headaches, psychosis, seizures, and cerebrovascular accidents.

Our study showed no significant variance in blood pressure of both groups. There were no abnormal findings in abdominal or CNS examination. However, pleurisy and pericarditis were significantly elevated in the cases group compared with the standard group, with 9 (15%) cases of pleurisy and 10 (16.67%) cases of pericarditis. In the cases group, there were 9 (15%) cases of pleurisy and 10 (16.67%) cases of pericarditis.

Our results from the study of Salam et al.[7] demonstrated that 15% of cases of SLE were pleurisy.

Our present study showed that all case groups were managed with steroids. Also, in the cases group, 8 (13.33%), 13 (21.67%), and 16 (26.67%) were managed with Azathioprine, Cyclophosphamide, and Hydroxychloroquine, respectively. No medicine was recorded in the

controls. All case groups were managed with steroids. Also, in the cases group, 8 (13.33%), 13 (21.67%), and 16 (26.67%) were managed with Azathioprine, Cyclophosphamide, and Hydroxychloroquine, respectively.

Our results were in line with those of Salam et al.[7], who demonstrated that 25% of cases were treated with a combination of cyclophosphamide and steroids, whereas 30% of cases were treated with steroids alone.

With treatment, 22 cases (out of 25 in the active nephritis group) in the study by Gaballah et al.[8] obtained complete (n = 3) or partial (n = 19) remission, as measured by a significant decrease in urinary IP-10 and sCD25 levels from baseline. None of the remaining three patients who failed to attain remission exhibited a comparable decline (p = 0.006 and p = 0.007, respectively). Completely remitted cases exhibited LN of classes II and III, whereas those who did not attain remission exhibited LN of classes IV+V.

Zeid et al.[11] corroborated our research findings, which documented that individuals with active LN exhibited elevated concentrations of urinary sCD25 in comparison to inactive patients and healthy controls. At a cutoff level greater than 27.9 ng/ml for sCD25, a Roc curve analysis revealed that it can distinguish significantly among active LN and lupus patients without activity, with a sensitivity of 84 percent and specificity of 65 percent. Patients with diffuse proliferative GN (class IV) exhibited the greatest urinary sCD25 levels, while cases in class II had the lowest levels. These levels correlated well with the activity and chronicity indices of renal biopsies. This may be accounted for because proliferative classes (III and IV) exhibit greater inflammation and T lymphocyte activation, which releases more sCD25. Furthermore, urinary sCD25 was positively correlated with renal biopsy activity ($r = 0.677$, $p < 0.001$; $r = 0.736$, $p < 0.001$) and chronicity indices ($r = 0.647$, $p < 0.001$; $r = 0.677$, $p < 0.001$).

Furthermore, a study done by Gupta et al.[12] examined 119 cases, of which 57 had active nephritis (AN), 43 had inactive disease (ID), and 19 had active non-renal (ANR). Urine and serum samples were collected for sCD 25 at baseline from all cases and at 3-month follow-up for cases with AN. At baseline, AN had significantly greater urinary sCD25 values than the inactive and control groups; however, the distinction was not statistically significant between the AN and ANR groups. The mean serum sCD25 concentrations of the three patient groups did not differ significantly at baseline. There was no correlation between urinary sCD25 levels and serum sCD25 levels. Nevertheless, no relationship was observed between urinary sCD25 and the protein: creatinine ratio in the urine.

The elevated levels of sCD25 detected in the urine of individuals with active LN are primarily the result of mesangial or mononuclear cells infiltrating the inflamed kidney rather than filtration from the circulation via the damaged glomeruli. Studies have demonstrated that active LN can be distinguished from quiescent disease based on urinary rather than serum sCD25 levels .[11]

On the contrary, Lin et al.[13] discovered a notable elevation in UsCD25 levels among patients diagnosed with active SLE, as assessed by the SLEDAI score, compared to those with inactive SLE. On the contrary, Bonelli et al.[14] and Zhang et al.[15]failed to identify an association between UsCD25 and disease activity, as measured by complement levels.

4. Conclusion

Because of its good association with several clinical and laboratory markers, urinary CD25 349.5 can be utilized as a noninvasive biomarker in assessing renal disease affection in patients with LN. Urinary sCD25 appears to be a promising biomarker for patient follow-up, with the capacity to predict recurrence and response to therapy, although blood sCD25 levels are not particularly effective. According to the results, local T cell activation in the kidney in LN appears to be active.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

References

1. André S, Conde B, Fragoso E, et al. COPD and Cardiovascular Disease. Pulmonology. 2019;25(3):168-176.
2. Sun L, Zhang L, Yu J, et al. Clinical efficacy and safety of anti-PD-1/PD-L1 inhibitors for the treatment of advanced or metastatic cancer: a systematic review and meta-analysis. Sci Rep. 2020;10(1):2083.
3. Gupta R, Yadav A, Misra R, Aggarwal A. Urinary sCD25 as a biomarker of lupus nephritis disease activity. Lupus. 2015;24(3):273-279.

4. Rosner MH, Perazella MA. Acute kidney injury in the patient with cancer. Kidney Res Clin Pract. 2019;38(3):295-308.
5. Mok CC. Biomarkers for lupus nephritis: a critical appraisal. J Biomed Biotechnol. 2010;2010:638413.
6. Das L, Brunner HI. Biomarkers for renal disease in childhood. Curr Rheumatol Rep. 2009;11(3):218-225
7. SALAM, Mohamed, et al. Urinary CD25 as a Biomarker of Lupus Nephritis Activity in Pediatrics. Geget, 2019; 14.1: 82-89.
8. Moroni G, Quaglini S, Maccario M, Banfi G, Ponticelli C. "Nephritic flares" are predictors of bad long-term renal outcome in lupus nephritis. Kidney Int. 1996;50(6):2047-2053.
9. Cameron JS. Lupus nephritis. J Am Soc Nephrol. 1999;10(2):413-424.
10. Hassan W, Behiry E, Mahgoub M. Urinary soluble alpha chain of the interleukin-2 receptor as a biomarker of active lupus nephritis in Egyptian children with juvenile systemic lupus erythematosus. Arch Rheumatol. 2020;36(1):47-55.
11. ZEID, Montasser Mohamed Hussein, et al. Study of urinary interferon gamma-induced protein 10 (IP-10) and urinary soluble CD 25 (sCD25) as markers of lupus nephritis and their relation to histological class. Alexandria journal of medicine. 2018; 54.4: 647-653.
12. Gupta R, Yadav A, Misra R, Aggarwal A. Urinary sCD25 as a biomarker of lupus nephritis disease activity. Lupus. 2015;24(3):273-279.
13. Lin CY, Hsu HC, Chiang H. Improvement of histological and immunological change in steroid and immunosuppressive drug-resistant lupus nephritis by high-dose intravenous gamma globulin. Nephron. 1989;53(4):303-310.
14. Bonelli M, Göschl L, Blüml S, et al. $CD4^{+}CD25^{-}Foxp3^{+}$ T cells: a marker for lupus nephritis?. Arthritis Res Ther. 2014;16(2):R104.
15. Zhang B, Zhang X, Tang FL, Zhu LP, Liu Y, Lipsky PE. Clinical significance of increased CD4+CD25-Foxp3+ T cells in patients with new-onset systemic lupus erythematosus. Ann Rheum Dis. 2008;67(7):1037-1040.