ОЦЕНКА УРОВНЯ CD163 В МОЧЕ КАК БИОМАРКЕРА ДЛЯ ДИАГНОСТИКИ ВОЛЧАНОЧНОГО НЕФРИТА

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Резюме. Цель работы – оценить мочевой CD163 как возможный биомаркер, указывающий на активность волчаночного нефрита (ВН). Проведено ретроспективное срезовое исследование в группе из 68 пациентов с диагнозом «системная красная волчанка» (СКВ) в течение 1 года, с учетом различных стадий волчаночного нефрита (ВН). Среди пациентов были 38 случаев с активным ВН, 15 – с историей ВН в неактивной фазе и 15 – без поражения почек. В исследовании использовали индекс SLEDAI для классификации активности заболевания, при этом активная ВН определялась по конкретным параметрам мочи. Биопсия почек проводилась у лиц с активной болезнью, в соответствии с установленными критериями классификации. Комплексная клиническая оценка включала анализы крови, уровни белка в моче и измерение мочевого sCD163 с помощью ИФА. При статистическом анализе применяли SPSS, используя различные тесты для сравнения групп и оценки взаимосвязи между уровнями sCD163 в моче и клиническими характеристиками, устанавливая достоверное различие при $p < 0,05$. Результаты исследования способствуют пониманию почечных проявлений при СКВ и потенциальной роли биомаркеров мочи в мониторинге прогрессии и активности заболевания. Были проанализированы лабораторные данные 68 участников с установлением корреляций между активным волчаночным нефритом (ВН), неактивным ВН и СКВ без поражения почек. Значимые корреляции ($p < 0,05$) наблюдались по содержанию CD163, C3, C4, уровням гемоглобина, тромбоцитов, сывороточного креатинина, протеинурии и азота мочевины, в то время как количество лейкоцитов, сывороточный альбумин и СОЭ не показали значимой корреляции. Примечательно, что 98,5% пациентов имели антитела к ds-ДНК. Уровни sCD163 в моче были самыми высокими у пациентов с активной ВН. Линейная регрессия показала, что сывороточный альбумин и СОЭ в значительной мере предсказывали уровни sCD163 в моче. Оптимальное пороговое значение для sCD163 в моче для прогнозирования почечной активности составило > 4,2 с чувствительностью 60,5% и специфичностью 66,7%. Однако уровни sCD163 не коррелировали с гистопатологией почек по принятой классификации. Внедрение определения sCD163 в моче в качестве биомаркера для оценки активности ЛН вместе с точной градацией по гистопатологическим классам нуждается в дальнейшей оценке. На данном этапе исследования sCD163 может быть хорошим показателем активности волчаночного нефрита. Однако sCD163 пока не может заменить биопсию почек при дифференциации ЛН по классам, поскольку она не обеспечивает достаточного понимания, необходимого для эффективного лечения ЛН.

Ключевые слова: системная красная волчанка, нефрит, CD163, биологический маркер

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EVALUATION OF URINARY CD163 LEVEL AS A BIOMARKER FOR THE DIAGNOSIS OF LUPUS NEPHRITIS

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Abstract. Aim of the work: to evaluate urinary CD163 as a possible biomarker indicating activity of lupus nephritis (LN). This retrospective, cross-sectional study evaluated 68 patients diagnosed with systemic lupus erythematosus (SLE) over a year, focusing on different states of lupus nephritis (LN). Participants included 38 with active LN, 15 with a history of LN in a non-active phase, and 15 without kidney involvement. The study utilized the SLEDAI index to classify disease activity, with active LN identified through specific urinary parameters. Renal biopsies were performed for those with active disease, following established classification criteria. Comprehensive assessments included blood tests, urinary protein levels, and measurement of urinary sCD163 using ELISA. Statistical analyses employed SPSS, utilizing various tests to compare groups and assess relationships between urinary sCD163 levels and clinical characteristics, establishing significance at $p < 0.05$. The findings contribute to the understanding of renal manifestations in SLE and the potential role of urinary biomarkers in monitoring disease progression and activity. Laboratory data from 68 participants were analyzed, focusing on correlations among active LN, inactive LN, and SLE without renal involvement. Significant correlations ($p < 0.05$) were observed in CD163, C3, C4, hemoglobin, platelets, serum creatinine, proteinuria, and BUN, while WBC count, serum albumin, and ESR showed no significant correlation. Notably, 98.5% of patients had positive anti-ds-DNA antibodies. Urinary sCD163 levels were highest in active LN patients. Linear regression showed that serum albumin and ESR significantly predicted urinary sCD163 levels. The optimal cut-off for urinary sCD163 to predict renal activity was > 4.2, with 60.5% sensitivity and 66.7% specificity. However, sCD163 levels did not correlate with renal histopathological classifications. Integration of urinary sCD163 as a biological marker for evaluating the activity of LN together with accurately distinguishing between histopathological classes mostly needs to be further evaluated. To this point of the study, sCD163 can be a good indicator of LN activity, sCD163 still can't substitute for renal biopsy in differentiation of LN classes as it would not provide the comprehensive understanding necessary for effective management of LN.

Keywords: lupus, nephritis, CD163, biomarker

Introduction

Systemic lupus erythematosus (SLE) Perhaps one of the most well-known ongoing autoimmune diseases, influences several organs, including the kidney, hematological system, skin, and joints [4].

Lupus nephritis (LN) is a common progression in up to 60% of SLE patients, with contrasting degrees of renal damage up to 17% percent of LN cases will eventually develop end-stage renal disease (ESRD) [7]. Since renal contribution is a significant indicator of prognosis, so early recognition of renal contribution in SLE cases is crucial to prevent the progression of ESRD [3, 20].

Although renal biopsy is currently considered the most reliable method for diagnosing and categorizing LN, it has limitations. It is an invasive procedure that cannot be repeated frequently to monitor treatment response, and the small tissue sample obtained may not fully represent the overall extent of kidney damage [4]. In contrast, urine samples are easily obtainable and offer a non-invasive approach to monitoring LN [5]. Non-invasive urinary biomarkers have the potential to serve as an alternative for evaluating LN [5]. While active sediments and proteinuria are commonly used as urine indicators of renal involvement, they have certain limitations [1]. For example, individuals with LN may have proteinuria, but the presence of leukocytes in the urine can indicate inflammation related to interstitial cystitis or urinary tract infection [5].

CD163 is a glycosylated transmembrane protein primarily expressed on tissue macrophages and subsets of circulating monocytes, as a scavenger receptor it is involved in hemoglobin clearance after hemolysis whether occurs in physiological or pathological scenarios [21]. It's considered a marker for M2 macrophages that have a beneficial role in resolving inflammation and aiding in injury recuperation [22].

Numerous glomerular disorders in humans, including diabetic nephropathy, ANCA-related vasculitis, post-streptococcal glomerulonephritis, and LN, are associated with CD163-positive macrophages [2]. Several systemic inflammatory conditions and autoimmune diseases are associated with increased CD163 levels in tissue as well as various body fluids according to the nature of the ongoing condition [8].

Peripheral blood serum and urinary CD163 amounts reflect the severity of the illness in cases of autoimmune disorders such as idiopathic inflammatory myositis, systemic sclerosis, and rheumatoid arthritis [19]. However, several investigations found a correlation between the severity of LN and urine-soluble CD163 [18].

The research **aimed** to survey whether urinary CD163 levels from cases suffering from LN could serve as a potential indicator of the disease's activity and to evaluate its ability to predict activity from active disease and even SLE patients without renal affection.

Material and methods

Patient selection and enrollment

We conducted a retrospective, cross-sectional study between March 1st, 2023, and February 1st, 2024. This study was carried out on 68 patients; 38 SLE with active LN, 15 participants with SLE who had previously experienced LN but were currently in a non-active state, and another 15 participants with SLE did not have any kidney inflammation. The participants were selected from both the outpatient clinic and the inpatient department of the Internal Medicine department in Tanta University Hospital; informed consent was taken from all patients included in the study. The study received approval from the ethics committees at both the Tanta and Kafr Elsheikh faculties of medicine. Before participation, all individuals were provided with a detailed explanation of the study's objectives and procedures, and informed consent was obtained from each participant involved in the study.

The systemic lupus international collaborating clinics (SLICC) classification criteria were used to diagnose systemic lupus erythematosus (SLE) and determine its activity. Clinical nephritis was suspected if the urine analysis revealed proteinuria exceeding 0.5 grams in a 24-hour urine collection, along with the presence of hematuria or cellular casts, with or without an increase in serum creatinine levels [24].

Exclusion criteria for the study included pregnant individuals, those with active infections, and individuals with other autoimmune diseases. The research received approval from the ethics committee at the Faculty of Medicine, Tanta University in Egypt.

Baseline assessments and measures

The assessment of disease activity in the study was carried out using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) [6]. Specifically, the renal SLEDAI was employed to evaluate the activity of kidney disease. This scoring system consists of four parameters associated with the kidneys: hematuria, pyuria, proteinuria, and urinary casts, with each parameter assigned a score of 4. Based on the results of the renal SLEDAI, patients were categorized as follows: those with active LN if their renal SLEDAI score was greater than 4, and patients with no renal activity in their SLE if they exhibited inactive kidney disease (renal SLEDAI = 0) during their clinic visit [6].

A total of 36 patients with active LN underwent renal biopsies, while patients with non-active LN and those without LN did not receive biopsies. The renal biopsies were classified according to the 2003 classification of LN established by the International Society of Nephrology and the Renal Pathology Society (ISN/RPS) [27].

All participants in this study underwent a series of procedures including taking their medical history, conducting a comprehensive clinical examination, and performing investigations at the Clinical Pathology Department in Kafrelsheikh University Hospital. Venous blood samples were collected from each patient using strict aseptic measures. The collected blood samples were utilized to conduct a range of tests, which encompassed a complete blood count (CBC), assessment of serum albumin, serum creatinine, blood urea nitrogen (BUN), and erythrocyte sedimentation rate. Additionally, the blood samples were analyzed for diagnostic markers of lupus, including anti-ds-DNA antibodies and serum complement levels (C3 and C4). Furthermore, a 24-hour urine sample was collected from each participant to measure 24-hour urinary protein levels.

Assessment of sCD163 levels

To measure urinary sCD163 levels, mid-stream urine samples were collected from all participants using sterile containers. For patients with active LN, urine samples were collected on the same day as the renal biopsy. The urine samples were then subjected to centrifugation at 2000-3000 rpm for 20 minutes. After centrifugation, the supernatant was carefully removed, divided into smaller portions (aliquoted), and stored at temperatures between -20 to -80 degrees Celsius for subsequent assessment of sCD163.

The quantitative determination of human sCD163 in urine was performed using an Enzyme-Linked Immunosorbent Assay (ELISA) Kit from DL Sci & Tech Development Co., Ltd., China. The specific catalog number for the ELISA Kit used was DL-CD163-Hu.

Statistical analysis

The data were analyzed using the IBM Microsoft Statistical Package for the Social Sciences (SPSS) version 22.0 software. The normality of quantitative data was assessed using Kolmogorov's test. Qualitative variables were presented using numbers and percentages, and the Monte Carlo exact test was employed for analysis when more than 20% of expected cell values were below 5. Numerical variables were reported as means and standard deviations or as medians with interquartile ranges (IQR). One-way ANOVA, Mann-Whitney U-test, and Kruskal-Wallis test were utilized to compare variables between groups. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic ability of urinary sCD163 in predicting renal disease activity

in SLE patients. Univariate linear regression analysis was conducted to evaluate the impact of various socio-demographic and clinical characteristics on urinary sCD163 levels in SLE patients. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic and laboratory data of the patients

Demographic and laboratory data including (CD163, C3, C4, hemoglobin, platelets, WBCs, serum albumin, serum creatinine, proteinuria, ESR, BUN, and The levels of anti-ds-DNA antibodies were compared among three groups: active LN, inactive LN, and patients without renal activity. The study consisted of 64 female and 4 male participants, with an average age of 37.73 years.

Significant correlation (p-value > 0.05) was found in CD163, C3, C4, hemoglobin, platelets, serum creatinine, proteinuria and BUN between the three groups, no significant correlation (p-value < 0.05) was found in WBCs count, serum albumin level nor ESR level

Out of 68 patients with SLE 67 (98.5%) patients had positive anti-ds-DNA; 38 of which were active LN patients (100.0% of active LN patients), 14 Non-active LN patients (93.3% of Non-active LN patients) and the rest 15 were SLE without nephritis patients (100.0% of SLE without nephritis patients) (Table 1).

Levels of sCD163 among the three groups showed a highly significant correlation, Active LN showed the highest levels when compared to non-active LN and SLE without nephritis (Table 1, Figure 1).

Impact of socio-demographic and clinical characteristics on urinary sCD163 levels in patients with systemic lupus erythematosus

A linear regression model was employed to examine the impact of socio-demographic and clinical characteristics on urinary sCD163 levels in patients with systemic lupus erythematosus. This analysis aimed to determine the extent to which these variables influenced the levels of urinary sCD163. Serum albumin and ESR were the main significant predictors found in this model with p values of 0.004 and < 0.0001 respectively (Table 2).

The ability of urinary sCD136 to predict renal activity

The optimum cut-off value for urinary sCD136 to predict renal activity was > 4.2 with a sensitivity of 60.5%, specificity of 66.7, the area under the curve

TABLE 1. CLINICAL CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH AND WITHOUT ACTIVE RENAL DISEASE

Clinical characteristics variables		All SLE (n = 68)	Active LN (n = 38)	Non-active LN (n = 15)	SLE without nephritis (n = 15)	p-value
Age (years)		37.73±12.37	36.89±14.19	40.73±8.53	36.86±10.73	0.421
Sex	Male	4 (5.9%)	0 (0.0%)	0 (0.0%)	4 (26.7%)	0.003*
	Female	64 (94.1%)	38 (100.0%)	15 (100.0%)	11 (73.3%)	
CD163 level (ng/mL)			5.38 (1.87-10.48)	4.8 (3.5-7.7)	1.1 (0.9-1.6)	< 0.0001*
Complement C3 (mg/dL)		24.0 (12.0-110.0)	18.0 (10.0-23.25)	114.0 (110.0-148.2)	102.5 (30.0-134.2)	< 0.0001*
Complement C4 (mg/dL)		14.0 (12.00-22.25)	14.0 (12.0-17.5)	23.5 (15.0-33.0)	13.5 (8.0-18.5)	0.013*
Haemoglobin (g/dL)		3.9 (1.4-5.9)	9.0 (8.3-10.0)	10.0 (9.0-13.0)	9.5 (8.5-11.0)	0.005*
Platelets (× 103/μL)		165.0 (150.0-189.0)	186.0 (158.0-210.0)	165.0 (150.0-175.0)	156.0 (125.0-175.0)	0.040*
WBCs (× 103/μL)		4.8 (4.1-6.4)	4.2 (3.7-5.4)	6.1 (4.3-6.4)	6.9 (3.1-8.3)	0.076
Serum Albumin (gm/dL)		4.0 (3.5-5.0)	3.5 (2.4-7.5)	4.0 (4.0-4.5)	4.5 (3.5-5.0)	0.408
Serum Creatinine (mg/L)		1.5 (0.9-1.9)	1.8 (1.5-2.6)	1.2 (0.9-1.6)	0.9 (0.8-0.9)	< 0.0001*
Proteinuria (g/24 h)		1.3 (0.4-4.0)	2.9 (1.8-4.8)	0.6 (0.4-1.0)	0.2 (0.1-0.2)	< 0.0001*
ESR (mm/1st h)		110.0 (100.0-110.0)	110.0 (107.0-110.0)	100.0 (10.0-115.0)	100.0 (90.0-110.0)	0.194
BUN (mg/dL)		65.0 (65.0-98.7)	65.0 (65.0-110.0)	65 (65)	65.0 (19.0-65.0)	< 0.0001*
+ ve anti ds-DNA		67 (98.5%)	38 (100.0%)	14 (93.3%)	15 (100.0%)	0.138

Note. *, significant. Values are presented as number (%), median (IQR) and mean±SD. SLE, systemic lupus erythematosus; ALN, active lupus nephritis; ILN, inactive lupus nephritis; NRA, no-renal activity; RBCs, red blood cells; WBCs, white blood cells; ESR, erythrocyte sedimentation rate; BUN, blood urea nitrogen; Anti-dsDNA antibody, anti-double stranded deoxyribonucleic acid antibody.

TABLE 2. COMPARISON OF URINARY sCD163 LEVELS WITH PATHOLOGICAL CLASSIFICATION OF RENAL BIOPSY IN ACTIVE LUPUS NEPHRITIS PATIENTS

Clinical characteristics variables		Univariate regression analysis	
		B (95% CI)	p-value
Age (years)		-0.11 (-0.54-0.31)	0.588
Sex	Female	8.49 (-13.92-30.90)	0.452
	Male	–	–
Complement C3 (mg/dL)		-0.07 (-0.17-0.03)	0.185
Complement C4 (mg/dL)		-0.08 (-0.23-0.07)	0.290
Haemoglobin (g/dL)		-0.09 (-3.37-3.18)	0.953
Platelets (× 103/μL)		0.02 (-0.05-0.10)	0.580
WBCs (× 103/μL)		-0.43 (-2.18-1.31)	0.619
Serum Albumin (gm/dL)		4.33 (1.45-7.22)	0.004*
Serum Creatinine (mg/dL)		1.34 (-4.64-7.34)	0.655
Proteinuria (g/24 h)		0.46 (-1.94-2.86)	0.703
ESR (mm/1st h)		-0.51 (-0.69 – -0.33)	< 0.0001*
BUN (mg/dL)		0.19 (-0.01-0.38)	0.051
+ ve anti-ds-DNA		7.97 (-35.98-51.93)	0.718

Note. Values are presented as median (IQR). LN, lupus nephritis; ALN, active lupus nephritis; ILN, inactive lupus nephritis.

TABLE 3. LINEAR REGRESSION MODEL FOR SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS AFFECTING URINARY sCD163 LEVELS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Renal biopsy LN class in … patients	Urinary sCD163 Median (IQR)
	Active LN (n = 36)
class III (n = 19)	5.3 (1.4-5.4)
class IV (n = 28)	10.4 (1.8-11.1)
class V (n = 1)	2.7
p-value	0.211

Note. *, significant. RBCs, red blood cells; WBCs, white blood cells; ESR, erythrocyte sedimentation rate; BUN, blood urea nitrogen; Anti-dsDNA antibody, anti-double stranded deoxyribonucleic acid antibody.

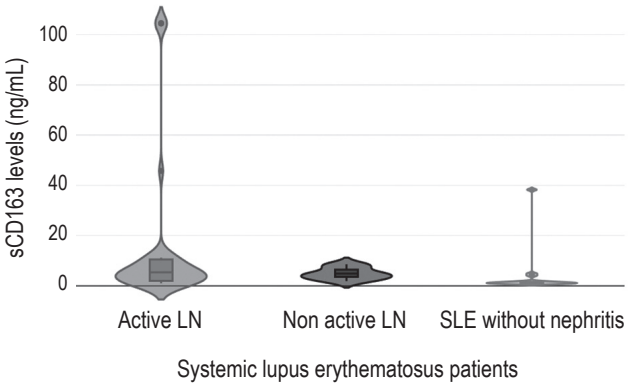

Figure 1. Violin plot for normalized urinary sCD163 levels in systemic lupus erythematosus patients

Note. LN, lupus nephritis; SLE, systemic lupus erythematosus.

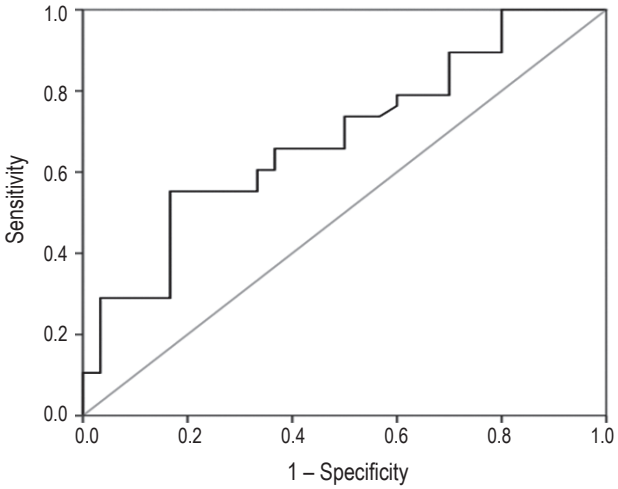

Figure 2. Receiver operating characteristic (ROC) curves for prediction active lupus nephritis by urinary sCD163 level

Note. The optimum cut-off value for urinary sCD136 to predict renal activity was > 4.2 with sensitivity 60.5%, specificity 66.7, area under the curve (AUC) 0.685, 95% confidence interval (CI) (0.558-0.811), p = 0.009.

(AUC) 0.685, 95% confidence interval (CI) (0.558-0.811), p = 0.009 (Figure 2).

sCD163 levels among different renal histopathological classes

When comparing sCD163 levels among different renal histopathological classes no significant correlation was found (p-value 0.211). Levels of sCD163 couldn't substitute renal biopsy in histopathological classification (Table 3).

Discussion

Adequately diagnosing active LN is the first step in proper control. Finding a biomarker with accepted sensitivity and specificity is a precious aim especially if this marker needs a non-invasive procedure to be evaluated and is easily estimated. Urinary biomarkers which may have more specific targeting of renal

affection compared with systemic ones are the main aim [26].

CD163 is a protein that acts as an indicator for the M2 phenotype of macrophages, being primarily found on their surfaces. It belongs to the scavenger receptor cysteine-rich (SRCR) superfamily and plays a crucial role in regulating inflammation and immune responses. The levels of urinary CD163 can be influenced by the proteolytic cleavage of these receptors, which occurs as a result of M2 macrophage activation [8, 15].

The main function of CD163 can be summarized as targeting apoptotic cells for removal and preventing the release of self-antigens that could trigger an autoimmune response. In cases of LN, the impaired clearance of apoptotic cells leads to the accumulation of self-antigens in the kidneys, which in turn stimulates the immune response [14, 17, 23]. CD163 expression is often upregulated in the presence of infection inflammation, or tissue injury, making it a useful marker for certain pathological conditions [25]. Macrophages have been implicated in the development and progression of Systemic Lupus Erythematosus (SLE).

Two main subtypes of macrophages, namely the classically activated inflammatory M1 macrophages and the alternatively activated M2 macrophages, have been identified. M2 macrophages exhibit pro-fibrotic, immune-regulatory, remodeling, and anti-inflammatory effects. G. Olmes et al. [23] conducted a study and found a higher presence of M2 macrophages and a lower presence of M1 macrophages across all classes of LN. These findings suggest that M2 macrophages may play a significant role in driving or regulating interstitial inflammation, cellular crescent formation, and fibrinoid necrosis, which are characteristic features of LN [11, 19]. Therefore, $CD163^+$ M2 macrophages are believed to be the predominant type of macrophage infiltrates in cases of LN.

In this study, the levels of urinary sCD163 were found to be significantly higher in patients with active LN compared to those with non-active LN, as well as in both LN groups compared to individuals with Systemic Lupus Erythematosus (SLE) but without nephritis. These findings align with the results reported by J.M. Mejia-Vilet et al. [19] and R. Gupta et al. [11]. The elevated levels of urinary sCD163 in active LN may be attributed to the local activation of M2 macrophages within the kidneys, leading to the production and release of sCD163 into the urine through proteolysis [8].

Regarding the prediction of renal activity, this study determined that a cutoff value of > 4.2 ng/mL for urinary sCD163 had a sensitivity of 60.5% and specificity of 66.7%. In contrast, N.M. Gamal et al. [10] obtained a higher sensitivity of 90.3% and specificity of 88.89% with a cutoff value of > 0.82 (U/mL/mg/dL). J.M. Mejia-Vilet et al. [19], on the other hand, identified a cutoff value of > 130 ng/mmol with a sensitivity of 97% and specificity of 94%. The variations in sensitivity and specificity among these studies may be attributed to differences in disease prevalence and patient populations, as these factors can influence the prevalence, sensitivity, and specificity of the diagnostic test [13].

Urinary sCD163 in this study showed a significant correlation with renal SLEDAI in predicting renal activity p value 0.009. This agrees with other studies that reported that urinary sCD163 has a significant role in predicting renal activity [11, 30].

When comparing results obtained regarding the capability of urinary CD163 levels to predict proliferative LN to other studies mentioning this point, our study disagrees with the majority in proposing a significant correlation [9, 11, 30]

In this study, a significant correlation was found between urinary sCD163 and serum albumin levels. This finding aligns with the results reported by N.M. Gamal et al. [10]. The correlation may be attributed to the fact that low levels of albumin are indicative of kidney injury. Additionally, the acute-phase response, which occurs during systemic inflammation, can affect albumin levels. Serum albumin is considered a negative acute-phase reactant, and its levels tend to decrease in response to inflammation [29]. A.A. Zeraati et al. [29] also found that lower albumin levels are significantly associated with higher disease activity in lupus. Furthermore, this study revealed a significant correlation between urinary sCD163 and erythrocyte sedimentation rate (ESR). This finding is consistent with the findings of Y.J. Huang et al. [12]. The elevation of ESR is commonly observed in inflammatory conditions, including autoimmune diseases. In patients with Systemic Lupus Erythematosus (SLE), higher ESR levels are often detected compared to C-reactive protein (CRP) levels. ESR elevations have also been strongly linked to disease exacerbations in SLE [16].

However, in contrast to the findings of Y.J. Huang et al. and J.M. Mejia-Vilet et al., this study did not find a significant relationship between urinary sCD163 and the presence of anti-ds-DNA antibodies [10, 12]. This can be explained by the fact that LN is initiated by the deposition of immune complexes containing anti-dsDNA antibodies in the kidney. However, the presence of immune complexes alone is not sufficient to induce renal injury, as additional immunological events are required to trigger kidney inflammation and damage [12].

In this study, no significant correlation was observed between urinary sCD163 and serum C4 levels. These findings are consistent with the results reported by N.M. Gamal et al. and Y.J. Huang et al., who also found no correlation between urinary sCD163 and C4 levels [19, 24]. Additionally, this study found no significant correlation between urinary sCD163 and serum C3 levels. This result

aligns with the findings of N.M. Gamal et al. [10] but differs from the observations made by T. Zhang et al. [30] and Y.J. Huang et al. [12] who reported a correlation between urinary sCD163 and C3 levels. The complex and intricate role of the complement system in the pathophysiology of LN contributes to this lack of consistent correlation. The complement system involves multiple activation pathways, numerous regulators, and genetic variations, making it challenging to establish a clear relationship. The complement system exhibits contradictory roles in LN, as it seems to play a protective role in preventing lupus initiation and disease activity through the classical pathway, while also contributing to tissue damage associated with LN [7].

The levels of urinary sCD163 showed variation across different pathological classes of active LN in patients who underwent renal biopsy, although this variation was not found to be statistically significant. This finding is consistent with the results reported by R. Gupta et al. [11] and N.M. Gamal et al. [10]. However, T. Zhang et al. observed a significant elevation of urinary sCD163 specifically in patients with proliferative LN [30]. This discrepancy in findings could be attributed to the fact that uCD163 is not specific to LN and its levels can be elevated in several other glomerular diseases. Consequently, uCD163 may be useful in identifying the inflammatory activity in LN, but only if other glomerular diseases are excluded [19].

To conclude CD163 is a promising biomarker for the diagnosis of active LN. Studies have shown that levels of soluble CD163 (sCD163) in the blood and urine are significantly elevated in patients with active LN compared to those with inactive disease or healthy controls.

Measuring sCD163 can help distinguish active from inactive LN, which is critical for guiding treatment decisions. Elevated sCD163 has shown good sensitivity and specificity for detecting active nephritis flares. It may also correlate with other markers of disease activity and could be used to monitor response to therapy.

Conclusion

Further research is needed to fully validate the clinical utility of sCD163 testing. However, the current evidence suggests it is a useful noninvasive biomarker that can complement other tests like kidney biopsies in the diagnosis and management of LN. Incorporating sCD163 measurement into the standard workup for these patients has the potential to improve outcomes.

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