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ORIGINAL ARTICLE

Urinary Monocyte Chemoattractant Protein-1 as a Diagnostic Marker of Lupus Nephritis

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Abstract

Background: **Systemic lupus erythematosus, sometimes known as SLE, is an autoimmune illness that can have far-reaching effects on bodily functions. Renal impairment is among SLE's most devastating effects. It affects 40—70 % of patients. One of the most important chemokines in attracting monocytes and macrophages to areas of inflammation is monocyte chemoattractant protein-1 (MCP1).**

Aim and objectives: **To determine if MCP-1 can aid in the early detection of lupus nephritis (LN) as well as look at any possible links among MCP-1 levels and disease severity in addition to kidney function.**

Patients and methods: **60 patients with ages ranging between 20 and 60 years were chosen from the Internal Medicine Department at both Al Hussein and Sayed Jalal University Hospitals and outpatient Clinic, with the appropriate consent to participate in this trial.**

Result: **There was significant variance between the 3 examined groups related to Renal and LN parameters and Urinary MCP-1 levels. There was no significant change amongst the three researched groups regarding age, sex, BMI and disease duration. There was a considerable positive and strong correlation amongst the MCP-1 with urea, ESR, proteinuria, anti-dsDNA, and renal SLEDAI.**

Conclusion: **Our findings show that urine monocyte chemoattractant protein-1 (uMCP-1) levels are much higher and correlate well with LN activity in persons with active Lupus nephritis, especially those experiencing a renal relapse. Active LN and/or recurrence might be distinguished from inactive renal disease by using urine monocyte chemoattractant protein-1.**

Keywords: Lupus nephritis (LN), Monocyte chemoattractant protein-1 (MCP1), Systemic lupus erythematosus (SLE)

1. Introduction

Multiple organs may be affected by systemic lupus erythematosus (SLE), an autoimmune illness. Renal failure is a major risk factor for SLE progression. It takes place in 40—70 % of all patients.[1]

Significant mortality and morbidity in people with SLE is attributable to lupus nephritis (LN).[2]

There have been many proposed markers in Egyptian individuals who have SLE that indicate renal dysfunction.[3]

One of the most important chemokines, monocyte chemoattractant protein-1 (MCP1) has strong chemotactic activity, drawing monocytes and macrophages to areas of inflammation.[2]

In Egyptian sufferers of SLE, MCP-1 was noticeably higher in individuals with a thicker intima media. Multiple cell types, including podocyte, mesangial, and monocyte cells, secrete MCP-1 as a reaction to factors that promote inflammation, such as tumor necrosis factor-alpha (TNF-alpha). These cells then mediate tissue damage and perform a function in the onset of renal failure.[2]

In individuals experiencing a renal flare, MCP1.

Levels in the urine have been reported to be considerably more elevated than those experiencing stable renal function.[4]

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2. Patients and methods

All persons were carefully chosen from the internal medicine department (at both Al Hussein and Sayed Jalal University Hospitals) and outpatient clinics, with appropriate consent to participate in this study.

MCP-1 levels were measured using the ELISA method in 60 people (ages 20–60) with LN (20 people who had active LN in addition to 20 individuals with inactive lupus nephritis) and 20 healthy participants serving as a control group.

2.1. Methods

All participants were exposed to the following workup: full history and clinical examination, evaluating the function of uMCP-1 in the early detection of LN also associating the levels with disease activity and renal status and valuation was used to define lupus activity and basic laboratory investigation; serological markers of activity (e.g.: C3, C4, Erythrocyte sedimentation rate (ESR)) signs of renal inflammation (e.g.; urinary sediments also 24 h urinary protein excretion rate).

2.2. Ethical consideration

The study was performed at the Outpatient Clinic of Al-Hussein University Hospital. Participants were asked to sign an informed consent form after having been given details about the procedure's potential risks in accordance with the guidelines set forth by the Institutional Review Board.

2.3. Statistical analysis

All data was entered into SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA) for tabulation as well as statistical analysis. The Shapiro–Wilk test was utilized to check for a normal distribution of the data. The qualitative information was shown as a breakdown of frequencies and %. The indicated variations among qualitative parameters were computed using the χ^2 test plus the Fisher exact test. Parametric quantitative information was displayed as mean SD (Standard deviation), while nonparametric data were shown as median range. When there were more than 2 groups to compare and the variables were normally distributed, researchers utilized the one-way ANOVA test. Parametric quantitative variables were analyzed using the Independent T-test and nonparametric variables were analyzed using the Mann–Whitney test.

When comparing the associations between variables, we used Spearman's correlation coefficient. We interpreted the plus sign as an indication of a direct correlation (in which a rise in the frequency of the independent variable results in an increase in the frequency of the dependent variable) and the minus sign as an indication of an inverse correlation (in which an elevate in the frequency of the independent variable results in a decrease in the frequency of the variable that is dependent). All tests for statistical significance involved using a three-tailed distribution. When comparing both groups, a *P*-value less than and equal to 0.05 is deemed significant, while a *P*-value below 0.001 is considered to be very significant, *P* higher than 0.05 indicates nonsignificant change.

3. Results

Table 1.

This table indicates: statistically, there is no alteration amongst the three studied groups according to age, BMI, sex and disease duration (Table 2).

This table demonstrates a highly significant statistical disparity in hemoglobin and PLT levels among the three groups (Table 3).

This table displays that there is a significant alteration amongst the three examined groups according to urea, proteinuria, creatinine, ESR and c reactive protein (CRP), C3, C4 also anti-dsDNA (Table 4).

This table shows that Monocyte chemoattractant protein-1 (MCP1) was significantly more elevated among active LN equated to inactive LN (Fig. 1, Table 5).

This table displays that there is a strong positive significant correlation amongst MPC-1 with urea, ESR, proteinuria, anti-dsDNA, and renal Systemic Lupus Erythematosus Disease Activity Index (SLEDAI).

Meanwhile, in the active LN group, MPC-1 correlates negatively and significantly with C3 as well as C4 (Fig. 2).

4. Discussion

Individuals with SLE are at a higher risk of dying or becoming disabled due to LN.[5]

Diagnosing LN is best done with a kidney biopsy. However, in clinical practice, repeat biopsies are not always feasible, especially for people who experience frequent relapses or who have significant hematologic or cerebral symptoms. In addition, persons with possible undetected coagulopathy, such as the existence of antiphospholipid

Table 1. Demographic data dispersal amongst the three investigated groups.

	Active LN ($N = 20$)	Inactive LN ($N = 20$)	Control ($N = 20$)	F/χ^2	*P*
Age (y) Mean ± SD	38.40 ± 9.54	37.62 ± 8.53	35.83 ± 6.9	0.493	0.613
Sex					
Male	2 (10 %)	1 (5 %)	4 (20 %)	2.26	0.322
Female	18 (90 %)	19 (95 %)	16 (80 %)		
BMI (kg/m^2) Mean ± SD	26.88 ± 2.54	25.23 ± 2.26	25.82 ± 2.73	2.21	0.119
Disease duration (yrs) Mean ± SD	4.52 ± 2.37	5.43 ± 2.84	–	1.2	0.282

Table 2. Laboratory parameters among the three investigated groups.

	Active LN ($N = 20$)	Inactive LN ($N = 20$)	Control ($N = 20$)	F	*P*
Hb (g/dl) Mean ± SD	11.12 ± 1.67	10.49 ± 1.81	13.18 ± 1.22	**16**	**0.000**
TLC (× 10^3/l) Mean ± SD	6.75 ± 2.04	6.13 ± 1.38	6.58 ± 1.69	0.691	0.506
PLT (× 10^3/l) Mean ± SD	257.32 ± 48.51	229.85 ± 62.15	288.35 ± 57.23	**5.42**	**0.007**
ALT (U/l) Mean ± SD	25.46 ± 5.54	27.32 ± 6.31	22.94 ± 5.86	2.77	0.074
AST (U/l) Mean ± SD	23.36 ± 5.33	25.48 ± 5.84	21.17 ± 5.34	3.06	0.055
T. bilirubin (mg/dl) Mean ± SD	0.674 ± 0.168	0.725 ± 0.173	0.59 ± 0.181	3.08	0.054
Albumin (g/dl) Mean ± SD	3.69 ± 0.31	3.94 ± 0.667	4.34 ± 0.382	3.07	0.054
INR Mean ± SD	1.04 ± 0.062	1.00 ± 0.055	1.03 ± 0.065	2.34	0.105

Table 3. Renal and lupus nephritis parameters between the three studied groups.

	Active LN ($N = 20$)	Inactive LN ($N = 20$)	Control ($N = 20$)	*P*
Creatinine (mg/dl) Mean ± SD	1.67 ± 0.648	1.36 ± 0.815	0.785 ± 0.173	**<0.001**
Urea (mg/dl) Mean ± SD	37.82 ± 6.24	22.55 ± 5.01	18.1 ± 4.21	**<0.001**
Proteinuria (mg/24 h) Mean ± SD	1849.5 ± 1237.1	985.9 ± 751.3	83.19 ± 24.52	**<0.001**
ESR (mm/h) Mean ± SD	130.71 ± 25.48	62.6 ± 33.39	11.75 ± 2.82	**<0.001**
CRP (mg/dl) Mean ± SD	24 ± 4.97	5.34 ± 3.71	2.11 ± 1.32	**<0.001**
C3 (mg/dl) Mean ± SD	52.93 ± 21.82	135.72 ± 57.3	103.35 ± 16.34	**<0.001**
C4 (mg/dl) Mean ± SD	8.65 ± 4.81	32.74 ± 14.31	30.81 ± 6.59	**<0.001**
Anti-dsDNA (mg/dl) Mean ± SD	112.37 ± 19.45	28.54 ± 7.45	4.43 ± 3.02	**<0.001**

Table 4. Urinary monocyte chemoattractant protein-1 levels between the three examined groups.

	Active LN ($N = 20$)	Inactive LN ($N = 20$)	Control ($N = 20$)	F	*P*
MCP-1 (mg/dl) Mean ± SD	1.06 ± 0.476	0.38 ± 0.154	0.24 ± 0.085	**34**	**0.000**

antibodies/antiphospholipid syndrome, or who are taking anticoagulants, should be aware that renal biopsy is a somewhat harmful operation linked with a significant albeit tiny risk.[6]

4.1. The main results were as followed

In our current trial demonstrated that there is no significant alteration among the three examined groups regarding age, sex, BMI in addition to disease duration (their age ranging between 20 and 60 years).

Our results supported by Alharazy and colleagues who wanted to measure and evaluate the levels of uMCP-1 in individuals with biopsy-proven LN at multiple stages of renal disease activity to check their accuracy against established markers. One hundred individuals with SLE who had LN confirmed by biopsy were included. In terms of age and sex, there was no statistically significant disparity among the two LN groups (the active and inactive ones).[6]

On contrast with our results Rosa and colleagues intended to use ELISA to evaluate urine monocyte chemoattractant protein-1 as a biomarker of renal activity in individuals with SLE and to correlate it to other markers for illness activity. There was a statistically significant variation in age amongst the groups. When compared with the R-LN and NR-

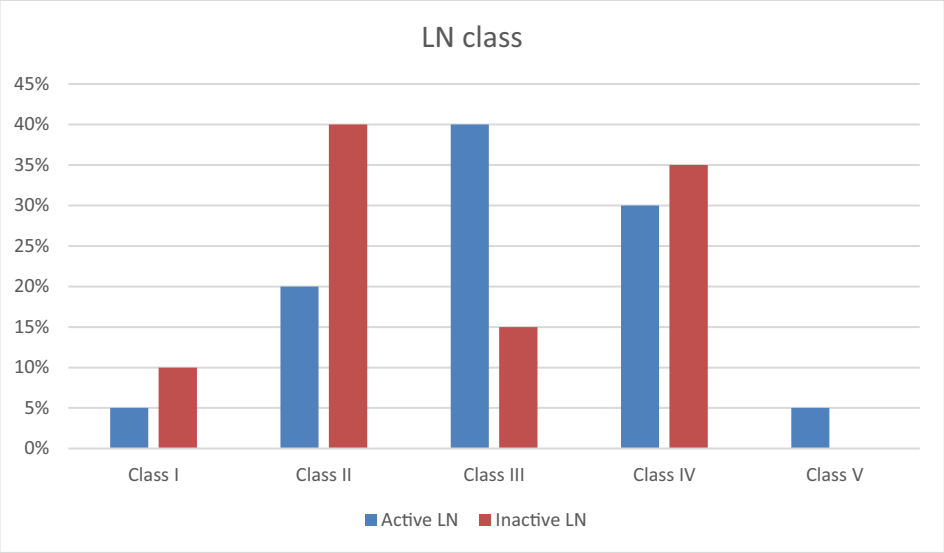

Fig. 1. Lupus nephritis class distribution among the two disease groups.

Table 5. Correlations between urinary monocyte chemoattractant protein-1 with lupus nephritis parameters in lupus nephritis groups.

Variable	Active LN (n = 20)		Inactive LN (n = 20)	
	R	*P*	r	*P*
Age	−0.060	0.750	0.056	0.764
BMI	0.077	0.681	0.077	0.681
Disease duration	0.262	0.154	0.059	0.751
Creatinine	0.341	0.078	0.221	0.232
Urea	**0.399**	**0.026**	0.299	0.183
Proteinuria	**0.453**	**0.005**	**0.426**	**0.011**
ESR	**0.416**	**0.018**	**0.362**	**0.025**
CRP	0.256	0.067	0.285	0.119
C3	**−0.533**	**0.007**	0.119	0.524
C4	**−0.492**	**0.009**	0.116	0.535
Anti-dsDNA	**0.644**	**<0.001**	**0.482**	**0.003**
Renal SLEDAI	**0.572**	**0.001**	**0.466**	**0.008**

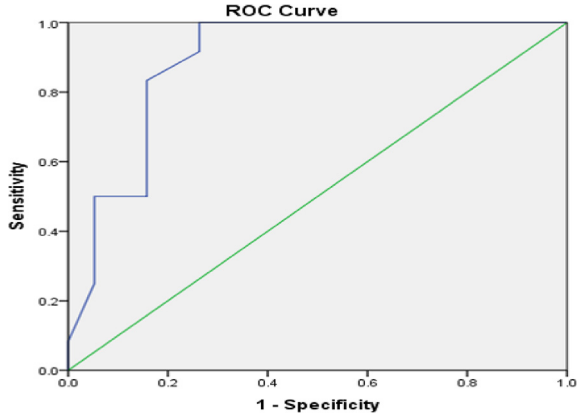

Fig. 2. Receiver operating characteristic curve for Urinary monocyte chemoattractant protein-1 as a marker for lupus nephritis.

SLE categories, the A-LN cohort was noticeably younger (*P* under 0.001).[7]

We noticed in the present research that there was a statistically significant change in hemoglobin, PLT andtotal leukocyte count among each group.

In contrast with our outcomes Zou et al. conveyed that there was no significance among the researched groups about platelets (PLTS) and Hemoglobin.[8]

This trial illustrated that there was a significant alteration amongst each of the three groups that were examined in creatinine, urea, proteinuria, ESR besides CRP, C3, C4 and anti-dsDNA.

On contrast with our results Ghobrial et al. who there were no statistically significant variances among groups A-LN as well as R-LN in terms of C3 besides C4 complement fragments, positive also negative anti-dsDNA outcomes, or serum creatinine, as reported. There were significant variations among the active along with inactive LN sets in terms of serum albumin (*P* less than 0.01), proteinuria (uPCI, *P* under 0.001) and proteinuria distribution (*P* below 0.001). After the research, serum creatinine had increased, but there were no disparities among both groups regarding anti-dsDNA Ab as well as serum complements (C3 and C4).[9]

On contrast with our results Radin and colleagues reported that there was no significance among groups regarding creatinine, C3, C4, and albumin.[10]

In our current study MCP-1 was significantly more among active LN compared with inactive LN.

Our results were supported by Alharazy and colleagues who reported urine monocyte chemoattractant protein-1 levels were significantly

increased in the active group as opposed to those in the inactive LN group.[6]

Also, our results supported with Mirfeizi and colleagues who reported that the mean value of urine MCP-1 levels in group 1 and group 2 were 144.16 ± 137.90 and 733.07 ± 1282.54 pg/ml respectively. In general, uMCP-1 level was significantly more in group 2 (with lupus nephritis) than in group 1 (without LN) ($P = 0.028$).[11]

Our results from this investigation indicate that there is a negative significant association amongst MPC-1 with C3 and C4 in the active LN group.

On contrast with our results Rosa and colleagues who indicated that nor did serum C3 and C4 values in A- LN provide a significant correlation with UMCP-1 levels ($P = 0.442$; $P = 0.868$, respectively).[7]

In our current study showed that uMCP-1 was significant in diagnosis of LN with cut off greater than or equal to 0.47 mg/dl, with a sensitivity of 91.7 % and specificity of 63.8 %, NPV of 79.3, and PPV of 83.5.

Also, our results were supported by Rosa and colleagues who reported that the data from the control group were used to determine an appropriate cutoff for employing this test to diagnose lupus nephritis. The percentage of A-LN with a positive uMCP-1 test was significantly more than in the other groups (P less than 0.001). Participants with SLE who also had renal involvement were utilized to establish a new cutoff for detecting disease activity in LN individuals. The test was only 50 % sensitive when specificity was set at 90 %.[7]

Also, El-Shehaby and colleagues noted that there are many chemokines involved in SLE, but uMCP-1 stands out as a very sensitive and specific biomarker of nephritic flares.[12]

In contrast with our results Abozaid and colleagues who reported that there was no significant change among the researched sets relating to renal SLEDAI.[13]

5. Conclusion

Regarding our results, Individuals with active LN, especially those experiencing a renal relapse, had considerably elevated uMCP-1 levels, which linked strongly with LN activity. UMCP-1 was able to distinguish amongst stable renal illness and inactive LN and/or recurrence. In terms of detecting LN activity and/or relapse, it consistently performed well, with good sensitivity and moderate specificity.

Authorship

All authors have a substantial contribution to the article.

Conflict of interest

The authors declared that there were NO conflicts of Interest.

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