Serum, Urinary and Tissue Monocyte Chemoattractant Protein 1 in Patients with Lupus Nephritis (A Comparative Study)

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Abstract: **Background*:*** Lupus Nephritis (LN) is one of the most common complications and is considered a crucial determinant of poor prognosis in Systemic Lupus Erythematosus (SLE) patients. Yet it is still a challenge for scientists to establish a sensitive and specific investigations that reflect renal status and can be linked to disease outcome and most importantly easy follow up with less hassle for the patient. ***Aim of the work:*** This study was done to estimate the serum and urinary Monocyte chemoattractant protein 1 (MCP-1) levels as non invasive markers in patients with SLE with comparison to tissue MCP1 and to evaluate the role of MCP-1 as an indicator for SLE disease activity and renal involvement (lupus nephritis).***Patients and methods****:* Serum and urinary MCP-1 were determined in forty randomly selected adult SLE patients their ages in years ranged from 17-54 (27.7± 7.9 years), the control group included twenty age and sex matched volunteers. SLE Disease Activity score (SLEDAI and the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index was recorded in all SLE patients. All patients were subjected to clinical and routine lab investigations. Serum and Urinary MCP1 were evaluated by ELISA technique. Renal biopsy was performed in Lupus nephritis patients for Histopathological classification, Activity and Chronicity indices and immunohistochemistry for MCP1 protein expression. ***Results:*** There was significant difference in level of urinary MCP 1 only in active than in inactive patients. In SLE with LN, serum and urinary MCP 1 showed a highly significant positive correlation with SLEDAI, proteinuria and serum creatinine and significant negative correlations with Hemoglobin. Urinary MCP1 showed highly significant difference between LN (class III&IV) and other classes of LN (p<0.001). Glomerular and tubulointerstitial MCP1 protein expression showed significant positive correlation with proteinuria (p=0.046 and 0.002 respectively).Tubulointerstitial MCP-1 protein expression showed significant difference between LN(class I, II, V) cases versus LN (class III, IV) cases (p=0.008) . Glomerular MCP1 showed highly significant positive correlation with activity index, while Tubulointerstitial MCP1 showed highly significant positive correlation with chronicity index (p <0.001). Urinary MCP1 showed positive significant correlation with both glomerular and tubulointerstitial MCP1 protein expression(p <0.001 and 0.016 respectively). Urinary MCP1 showed highly significant correlation with activity index (p <0.001), while Serum MCP1 showed no significant correlation with activity or chronicity indices**.** ***Conclusion:*** MCP1 could be a valuable marker for LN and can help in assessment of disease outcome and follow up of patients, furthermore, Urinary MCP1 in our study proved to be a sensitive , non invasive tool for assessment of LN patients that can be linked to Histopathological classes and tissue MCP1 protein expression.

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1. Introduction

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disorder that may affect multiple organ systems. Renal damage is one of the most serious complications of SLE. The majority of people with lupus have some degree of asymptomatic microscopic kidney damage. Renal involvement occurs in 40% to 70% of all patients[(1)].

While autoantibody production and complement activation are the major players in initiating the inflammatory response in lupus nephritis (LN), cellular immune mechanisms mediated through infiltrating mononuclear cells have an important role in progression of renal injury[(2)].

Chemotactic factors, such as monocyte chemoattractant protein-1 (MCP-1), appear to play a pivotal role in leucocyte entry into the kidney, enhancing endothelial and leucocyte adhesiveness and endothelial permeability in murine and human LN. This has been proven by previous immunohistochemical and *in situ* hybridization analyses of renal tissue from patients (or experimental animals) that have demonstrated local renal expression of chemotactic factors in association with inflammatory disease[(3)].

All types of renal cells (endothelial, mesangial, tubular epithelial, interstitial cells, and podocytes) can express chemokines upon stimulation. Proinflammatory stimuli, such as TNF-α, IL-1, IFN-γ

and lipopolysaccharide (LPS), within a few hours induce MCP-1, this may represent a common mechanism of injury-induced chemokine generation[4].

There is an increasing body of evidence that MCP-1 plays a major role in the pathogenesis of progression of renal disease. This is based on observations both in various animal models of renal damage and in different types of human renal disease[5].

The presence of chemokines in the urine of patients with SLE nephritis may reflect intrarenal chemokine expression[6].

This study was designed to estimate the serum and urinary MCP-1 levels as noninvasive markers in patients with SLE with comparison to tissue MCP1 protein expression and to evaluate the role of MCP-1 as an indicator for SLE disease activity and renal involvement (lupus nephritis).

2. Patients and methods

2.1 Study Subjects and Design

The current study was observational cross sectional study. Sample was estimated to be forty adult SLE patients (37 women and 3 men), collected by systematic random method. All patients were collected from Rheumatology & Rehabilitation department in Zagazig University Hospitals, in the period from October 2010 to November 2011.All investigations were done in Clinical Pathology and Pathology Departments in Zagazig University. Patients ages ranged from 17 and 54 years of mean ± SD (27.7± 7.9years), disease duration ranged between 0.5 and 14 years of mean ± SD/ (3.6± 3.0 years). Twenty (18 females and 2 males) apparently healthy volunteers were included as controls, they were age and sex matched with the patients, their ages ranged from 20 and 50 years of mean ± SD /years was (26.7 ± 8.0 years).

SLE patients fulfilled at least four of recent SLE criteria described by **Petri , [7].** SLE Disease Activity was based on the SLEDAI score amended in 2000[8]**),** patients with a score ≤ 4 were considered inactive while those with a score > 4 were considered active. The Systemic Lupus International Collaborating Clinics (SLICC) Damage Index, which has been endorsed by the American College of Rheumatology, was also used[9]**.**

Twenty out of the 40 patients were diagnosed as lupus nephritis according to SLE criteria: proteinuria ≥ 500 mg/day and/or red cell casts[7]. The diagnosis of renal involvement was confirmed in them by renal biopsy.

Lupus treatment at the time of serum sampling involved low-dose prednisolone (<0.5 mg/kg/day) in thirteen patients, high-dose prednisolone (≥ 0.5 mg/kg/ day) in twenty seven patients, intermittent intravenous cyclophosphamide in eighteen patients, oral azathioprine in twenty one patients.

Individuals with urinary tract infection were excluded by doing urine culture for all those with pyuria.

Ethical consideration: A written consent was taken from all of the participants after explaining details, benefits as well as risks to them.

2.2. Laboratory procedures

Laboratory investigations were done for all subjects including:

1- Complete blood count (CBC), Erythrocyte sedimentation rate (ESR), Complete Urine analysis together with quantitative 24 hours urinary protein excretion.
2- Complement C-3 (turbidimetric assay).
3- Antinuclear antibody (ANA) and Anti-dsDNA Ab were done by the indirect immunoflorescence technique.
4- **Monocyte chemoattractant protein 1 by ELISA technique :** Estimated in Urine and Serum.

It was done by Quantikine kit for Human MCP-1/CCL2 immunoassay (R&D Systems, Inc., USA) according to manufacturer description.

After the procedure The optical density was determined using ELISA reader (Teco-96 microplate reader, USA) set to 450 nm. To correct for optical imperfections in the plate, wavelength correction was set to 630 nm.

According to the manufacturer samples taken from healthy volunteers MCP1 in serum ranged from 200 to 722 pg/mL and in Urine from 42 to 410 pg/mL. In our study urine values were normalized for creatinine content by division of value of urine MCP-1 by pg/mL on value of urine creatinine by mg/dL.

5- Renal biopsy:

a) Histopathology: percutaneous renal biopsies taken only from lupus nephritis patients (n = 20) were evaluated according to the World Health Organization (WHO) classification of lupus nephritis[10]. The activity index (AI) and chronicity index (CI) of each biopsy specimen were scored by standard methods[11]**.** The distribution of histopathological classification of patients in this study was: class I, 1 (5%); class II, 4 (20%); class III, 7 (35%); class IV, 6 (30%); class V, 2 (10%) cases. The mean values for activity and chronicity indices of class III and IV were 6.9 ± 5.7 and 4.0 ± 3.1 respectively.

b) Immunohistochemistry:

Immunohistochemical staining was carried out using streptoavidin-biotin immunoperoxidase technique (Dako-cytomation, CA). Three to five micrometer thick sections, cut from formalin fixed

paraffin embedded blocks, were deparaffinized in Xylene and rehydrated in graded alcohol. Sections were boiled in citrate buffer (pH 6.0) for 20 min and then washed in phosphate buffer saline (pH 7.3). Then blocking of endogenous peroxidase activity by 6% H_2O_2 in methanol was attained. The slides were then incubated over night with the monoclonal anti-MCP-1 antibody (R&D systems, Oxon, UK). negative controls, obtained by substitution of primary antibodies by blocking buffer were included in the staining procedure. Incubation with secondary antibody and product visualization was performed employing (Dako Cytomation, Glostrup, Denmark) method with Diaminobenzidine (DAB) substrate chromogen. Slides were finally counterstained with Mayer's haematoxylin. Glomerular and tubular staining of biopsies were analysed using a modified histopathology score (H-score of 100–300) based on both percentage of positively stained cells and a semi-quantitative scale of immunointensity (0 = negative, 1 = mild, 2= intermediate, 3 = strong), scores ≤ 100 were considered negative[12].

Statistical methods: Data was analyzed using SPSS win statistical package version 15 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation (SD) or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data, comparison between two groups was done using Mann-Whitney test. Comparison between 3 groups was done using Kruskal-Wallis test. Spearman-rho method was used to test correlation between numerical variables. p-value < 0.05 was considered significant.

3. Results

3.1 Demographic and laboratory data of all studied subjects

Significant difference was detected comparing selected laboratory data of patient groups versus control group (P < 0.001). All laboratory data were significant when comparing SLE patients with LN to those without LN except serum MCP1 showed no significant difference between them (Table 1).

Table 1 Comparison between SLE patients with and without lupus nephritis

		Control (No=20)	SLE without LN (No=20)	SLE with LN (No=20)
Sex	Female n.%	18(90)	19 (95)	18 (90)
	Male n.%	2(10)	1 (5)	2 (10)
Age /years Median (Range)		29 (20-54)	26 (17-33)	27 (16-50)
SLEDAI ≤ 4	n.%	-	15*	1
Serum creatinine (mg/dl)		0.8±0.3	0.75 ±0.16	2.1 ±1.6*
Urine creatinine (mg/dl)		106.40 ±52.43	194.1 ±167.7	82.2 ±34.9*
Hemoglobin (g/dl)		12.0 ±1.3	12.4 ±1.5*	8.7 ±1.7
Proteinuria (g/24h)		0.048±0.023	0.271±0.16	2.118 ±1.35*
Serum MCP1 (pg/dl)		237.5±14.6	622±536	673±465
Urinary MCP1 (pg/mg creatinine)		1.2±0.1	2.2 ±2.4	28.5 ±25.0*

Significant when comparing SLE with LN versus SLE without LN
* Significant when p<0.05

3.2 Comparison between SLE patients as regard SLEDAI

SLEDAI recorded significantly higher scores in active than inactive patients. There was significant difference in level of urinary MCP 1 only in active than in inactive patients (Table 2).

Table 2. Clinical and laboratory parameters in SLE patients according to SLEDAI

	Inactive SLE (n = 16) Score ≤ 4	Active SLE (n = 24) Score >4	P
Serum MCP1(pg/dl)	709.75 + 460.49	871.46 + 439.44	0.255
Urine MCP1(pg/mg)	1.57 + 1.35	24.51 + 24.48*	0.001
SLEDAI	3.09 ±1.0	14.26 ±4.21*	<0.01
SLICC/ACR	4.1±1.0	4.4±0.7	>0.05

* Significant when p<0.05
* Significant difference comparing active versus inactive SLE patients
SLEDAI :Systemic Lupus Erythematosus Activity Index
SLICC: The Systemic Lupus International Collaborating Clinics Damage Index

3.3 Correlation between serum and urinary MCP 1 and different laboratory and clinical parameters

Urinary MCP 1 showed a significant positive correlation with proteinuria in SLE patients with and without LN but there was no correlation between serum MCP and proteinuria in both groups.

In SLE with LN, serum and urinary MCP 1 showed a highly significant positive correlation with SLEDAI, proteinuria and serum creatinine ($P < 0.001$), they had significant negative correlations with Hemoglobin ($P < 0.05$) (Tables 3 & 4).

Table 3. Correlation between serum and urinary MCP 1 and different laboratory and clinical parameters in SLE without LN

	Hemoglobin	Serum creatinine	SLEDAI	Proteinuria
Serum MCP 1	-0.092	0.104	-0.115	0.461
Urinary MCP 1	-0.013	0.547*	0.249*	0.565*

* Significant when $p<0.05$

Table 4. Correlation between serum and urinary MCP 1 and different laboratory and clinical parameters in SLE with LN

	Hemoglobin	Serum creatinine	SLEDAI	Proteinuria
Serum MCP 1	-0.441*	0.376	-0.191	0.489
Urinary MCP 1	-0.613*	0.532*	0.587*	0.666*

* Significant when $p<0.05$

3.4 Comparison between class I, II, V cases and class III, IV cases as regards (tissue, urinary and serum) MCP1 and different lab paremeters.

Glomerular MCP-1 protein expression showed near significant difference (P-value = 0.157) between class I, II, V cases versus class III, IV cases (mean value 103.1 ± 3.6 and 157.5 ± 54.9 respectively). Meanwhile tubulointerstitial MCP-1 protein expression showed significant difference (P-value = 0.008) between class I, II, V cases and class III, IV cases (mean value 102.6 ± 4.4 and 155.2 ± 43.9 respectively) (Fig. 1).

As regards urinary MCP1 and serum MCP1, only Urinary MCP1 showed highly significant difference between class III&IV and other classes of LN ($p<0.001$).

3.5 Correlation between MCP-1 protein expression in tissues and clinicopathological features in SLE patients with lupus nephritis.

Both Glomerular and tubulointerstitial MCP1 protein expression showed significant positive correlation with proteinuria(p=0.046 and 0.002 respectively). (Table 5)

Table 5. Correlation between MCP-1 protein expression in tissues and Lab parameters:

	Glomerular MCP-1 score	Tubulointerstitial MCP-1score
Creatinine (mg/dl)	0.287	0.241
Proteinuria (g/24h)	0.452*	0.656*

Values presented are correlation coefficient "r"

* Significant when $p<0.05$

**Highly significant when $p<0.001$

3.6 Correlation between MCP-1 protein expression and urinary and serum MCP-1 level in cases of SLE patients with lupus nephritis:

Urinary MCP1 showed positive significant correlation with both glomerular and tubulointerstitial MCP1 protein expression (p <0.001 and 0.016 respectively) (Table 6).

Table 6. Correlation between MCP-1 protein expression and urinary and serum MCP-1 level:

	Glomerular MCP-1 score	Tubulointerstitial MCP-1score
Urine MCP-1	0.802**	0.530*
Serum MCP-1	0.189	-0.054

* Significant when $p<0.05$

**Highly significant when $p<0.001$

3.7 Correlation between urinary MCP1 and serum MCP1 and both activity and chronicity indices in lupus nephritis patients in ISN/RPS class III and IV together.

Urinary MCP1 showed highly significant correlation with activity index (p <0.001), while it shoed no significant correlation with chronicity index. Serum MCP1 showed no significant correlation with activity or chronicity indices. Glomerular MCP1 protein expression showed highly significant positive correlation (p <0.001) with activity index , while Tubulointerstitial MCP1 immunoreactivity showed highly significant positive correlation (p <0.001) with chronicity index. (Table 7)

Table 7. Correlation between urinary MCP1 and serum MCP1 and both activity and chronicity indices in lupus nephritis patients in ISN/RPS class III and IV together.

	Urine MCP1	Serum MCP1	Glomerular MCP1	Tubulointrerstitial MCP1
Activity index	0.953**	0.536	**0.966****	0.181
Chronicity index	0.155	0.330	0.108	0.980**

* Significant when p<0.05

**Highly significant when p<0.001

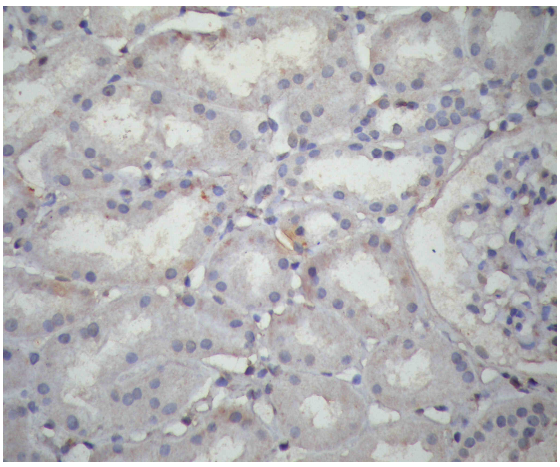

Fig.1 (A)

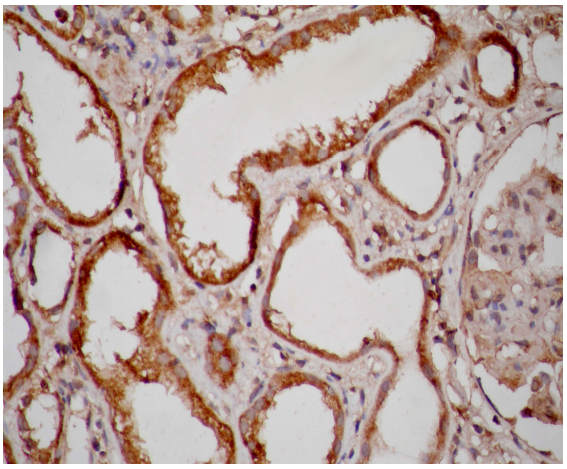

Fig.1 (B)

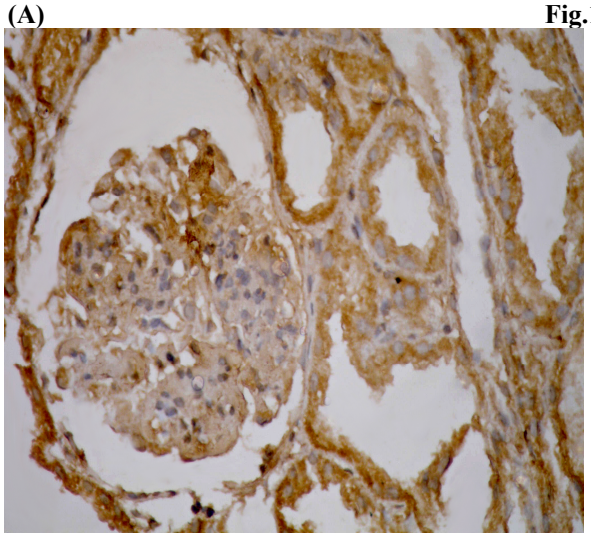

Fig.1 (C)

Fig.1: A- Faint (negative) cytoplasmic MCP-1 immunoreactivity in glomerular & tubulointerstitial tissue (original magnification x 400); **B-** moderate glomerular and strong tubulointerstitisal MCP-1 immunoreactivity (original magnification x 400); **C-** strong glomerular and moderate tubulointerstitisal MCP-1 immunoreactivity (original magnification x 400).

4. Discussion

Renal involvement is one of the main determinants of poor prognosis of SLE [13] Cellular immune mechanisms mediated through infiltrating mononuclear cells have an important role in amplification and progression of renal injury[1]. The disease course of LN is highly variable and multiple clinical, serological, histopathological and time dependent factors are responsible for its ultimate prognosis[14]. Novel biomarkers must be judged against an activity measurement that is superior to kidney biopsy[15].

In the present study, we evaluated urine and serum MCP1 as noninvasive markers and we tested them against tissue MCP1 protein expression in relation to different lab parameters, and we compared different histopathological classes as regards all types of MCP1. Moreover correlation studies were used to find the association between MCP1 and activity or chronicity indices in an attempt to find out different types of MCP1 association with disease outcome.

We found out that serum MCP-1 level was higher in SLE patients than controls. No statistically significant difference was found between SLE Patients with and without LN. This is in agreement with the results also obtained by **Li *et al*.**[16], they found that the serum MCP-1 levels were very high in many patients with SLE when compared to controls.

This was also in agreement with the results obtained by other researchers[17] who found that in SLE Patients with renal involvement the mean value of serum MCP-1 was significantly higher than healthy subjects, no statistically significant difference between SLE patients with and without renal affection.

A previous study[18] concluded that MCP-1 levels in sera of both active phase and remission phase of LN patients were markedly higher than those in controls and there no significant difference was found between the patients of active and remission phase.

We found that the mean value of urine MCP-1 in SLE patients with LN was significantly higher than those patients without LN (p<0.001) and also significantly higher than controls (p<0.001). There was no statistically significant difference between SLE patients without LN and controls (P = 0.840); this is in agreement with the results obtained by other studies[19], [20].

Li and colleagues[18] agreed with us that the MCP-1 levels in urine of active phase patients were markedly higher than those in controls, but no significant difference was found between the MCP-1 levels in urine between the remission phase patients and control.

It was found that urinary MCP-1 of patients with renal flare was significantly higher than that of healthy control subjects and higher than SLE patients with non-renal flare[21,22]) and this also was similar to our study.

There is a general agreement in different literatures that the more active classes of biopsy proven LN are class III and IV, while other classes, namely class I, II, V and VI are considered less active that needs limited immunosuppressive therapy [23].

In the present study, Urinary but not serum MCP 1 levels were significantly higher in SLE patients with lupus nephritis (biopsy class III and IV together) than (biopsy class II and V together).

Tucci *et al.*[6] found that urinary levels of MCP-1 were markedly elevated in patients with LN and were correlated with the histologic class of nephritis, and they stated that elevation of urinary MCP-1 levels in patients with active LN, along with a decrease in urinary MCP-1 levels after successful treatment. This may suggest that MCP-1 overproduction is due to an inherent defect in patients with LN. Further support of this hypothesis may be the strong influence of the MCP-1 genotype on urinary MCP-1 levels, and they emphasized that ,as evidence against a constitutive up-regulation of MCP-1 in patients with LN, they found a marked decrease in urinary MCP-1 levels during treatment with cyclophosphamide.

We agreed with previous studies [24,25] that the Level of UMCP-1 was significantly correlated with total SLEDAI score however there was no correlation between serum MCP-1 and this score,

Urinary MCP 1 showed a significant positive correlation with proteinuria in SLE Patients with and without LN, but there was no correlation between serum MCP and proteinuria in both groups. This was in agreement with other researchers[4,24] who found that UMCP-1 correlated with the extent of proteinuria. Some patients had persistently elevated UMCP-1 despite improvement in proteinuria, suggesting the possibility of ongoing subclinical inflammation in the kidneys[26].

In this study there was a positive correlation between UMCP-1 and serum creatinine in both groups of SLE patients, this was similar to study of **Tucci *et al.*[6]** who found that there was negative significant correlation between both serum and Urinary MCP-1 and hemoglobin in SLE patients with and without LN, also this is in agreement with the results obtained by **other researchers**[21]. This suggests that measurement of urinary chemokines may be a noninvasive method for the assessment of the severity of lupus nephritis[4].

Our study demonstrated increased urinary MCP-1 levels in patients with Lupus nephritis compared to Lupus non-nephritis patients. Urinary MCP-1 levels correlated with SLE disease activity. There were no differences in serum MCP-1 levels between those patients with and without LN. With the

measurement of urinary levels of MCP-1, it shows a positive correlation with proteinuria and thus being a useful tool for the detection and management of LN.

It was explained in previous researches[27] that The lack of significant increase of circulating levels of MCP-1 in serum of patients with nephritis is due to the possibility that locally produced MCP-1 is excreted into urine rather than circulated in the blood, and to the extremely short half-life of MCP-1 in serum .Furthermore **Li *et al.*[16]** stated that urinary MCP-1 levels reflect predominantly local production of this chemokine rather than simply filtration of MCP-1.

In our study renal biopsy was obtained from SLE patients with lupus nephritis and MCP1 protein expression in tissues was evaluated in relation to different lab parameters, urinary and serum MCP1.

No relationship was noted between serum creatinine and either glomerular or tubulointerstitial MCP-1 protein expression. **Marks and colleagues[28]** found no relationship between glomerular MCP-1 and serum creatinine.

A significant relationship was noted between the level of proteinuria and both glomerular and tubulointerstitial MCP-1 immunoreactivity.These findings were similar to those from a previous study[28] that showed a significant relationship between protein level in urine and glomerular MCP-1 . proteinuria stimulates renal tubular epithelial cells to produce cytokines such as MCP-1 that can contribute to chronic kidney damage[29]**.** However other studies reported no association between the degree of proteinuria and MCP-1 expression[30,3]**.** This discrepancy may be because all their cases had mild proteinuria < 3.5 gm/ day, however, sever proteinuria may be associated with tubulointerstitial damage.

There was a paucity of glomerular expression of MCP-1 in ISN/RPS class I, II and V. however, patients with class III and IV lupus nephritis had over-expression of glomerular MCP-1 protein with near significant difference compared to other classes (P = 0.157). This is in agreement with **Marks *et al*.[28]** who showed significant difference in MCP-1 expression between classes III & IV versus classes I, II & V

In the present study , there was a highly significant correlation between Activity index of lupus nephritis patients ISN/RPS classes III , IV and glomerular MCP-1 protein. This is in agreement with previous studies[3,28] who reported a significant association between histopathological activity of lupus nephritis and glomerular MCP-1 protein expression. These findings are consistent with previous findings showing increased MCP-1 staining in glomerular and interstitial cells in human crescentic glomerulonephritis[31]**.**

Regarding the correlation between tubulointerstitial MCP1 protein expression and Chronicity index of lupus nephritis patients ISN/RPS classes III , IV, a highly significant correlation was found in our study.

Consistent with our findings, **Chan *et al.*[3]** found significant correlation between chronic renal damage represented by histopathological chronicity index and tubulointerstitial expression of MCP-1 (P = 0.015), which is consistent with the current understanding of pathophysiology of chronic kidney disease[32]**.** Also **Dai *et al.*[30]** reported tubular of MCP-1 was strongly associated with monocyte infiltration and fibrosis in interstitium of lupus nephritis patients, suggesting that upregulation of tubular MCP-1 may initiate the process of monocyte recruitment and thus leads to interstitial fibrosis. **Wada and Furuichi[33]** suggested that MCP-1 expression contributes to interstitial fibrosis in human crescentic glomerulonephritis.

There was a highly significant positive correlation between activity index and urinary MCP1 while it showed no significant correlation with Serum MCP1. Chronicity index didn't correlate with any of them. Similarly, **Zhu *et al.*** (34) reported a positive correlation between urinary MCP1 and histopathological activity index, but not chronicity index.

A significant positive correlation was found between urinary MCP-1 and tissue MCP-1 protein expression, whether glomerular or tubulointerstitial, while another study[31] reported no association between urinary and tubulointerstitial MCP-1, but strong association between urinary MCP-1 and glomerular macrophage infiltration. No association was found between serum MCP-1 and neither glomerular nor tubulointerstitial MCP-1. This is in agreement with study done by **Dai *et al*.[30]**

Therefore, MCP-1 may have a role in the etiopathogenesis of LN and could be utilized as a potential biomarker of disease activity. therapeutic strategies with MCP-1 antagonists to ameliorate the initiation and progression of disease would be beneficial as future possible treatments. This has been demonstrated in murine (MRL lpr mice) LN [35]. In addition, anti-MCP-1 gene therapy in murine LN offers protection against renal injury due to reduced infiltration of leucocytes by significantly reducing glomerular IL-12 mRNA production and interstitium-infiltrating cell production of IL-12 and IFN-gamma mRNA [36].

Conclusion

MCP1 could be a valuable additional tool to diagnose LN and will certainly help us to suspect LN, diagnose it earlier and monitor nephritis activity in the follow up. Urinary and not serum MCP1 is a useful

non-invasive marker for the assessment of renal disease in patients with lupus nephritis.

Disclosure of Interest: None declared

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