Urinary and Plasma Monocyte Chemotactic Protein 1 as a Predictive Markers of Steroid Responsiveness in Children with Idiopathic Nephrotic Syndrome

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Abstract

Background: Idiopathic nephrotic syndrome (NS) is one of the most common kidney diseases in children and is characterized by heavy proteinuria, hypoalbuminemia, edema, and hypercholesterolemia. Most cases of idiopathic NS are steroid sensitive; however, some cases become steroid-resistant during their clinical course. The objective of this study was to investigate the diagnostic value of plasma and urinary MCP-1 in pediatric patient with idiopathic nephrotic syndrome, to detect effect of disease remission and activity on these levels and to compare our results between case of age and sex matched control group. Methods: This case control study was conducted at Pediatrics nephrology unit, pediatric nephrology outpatient clinic at Zagazig university hospitals on Children attending at pediatric inpatient and outpatient clinic. They were classified into: Group A: This group included 27 nephrotic patients in remission. Group B: This group included 27 nephrotic patients in activity either with 1st attack or relapses. Control group: This group included 27 age and sex matched healthy children attending general pediatric clinic. Results: There is statistically non-significant difference between the studied groups regrading hemoglobin, white blood cells, or platelet count. In our study, there is statistically non-significant difference between the studied groups regarding serum urea or creatinine. In this study, there is statistically significant difference between the studied groups regarding both serum albumin and total cholesterol (on doing posthoc test, the difference is significant between each two individual groups). In our study, there is statistically significant difference between the studied groups regarding Urinary Monocyte Chemotactic Protein 1 (on doing posthoc test, the difference is significant between each two individual groups). The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of nephrotic syndrome is ≥79 with area under curve 1, sensitivity 100%, specificity 96.3%, positive predictive value 98.2%, negative predictive value 100%, and overall accuracy 98.8%. The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of steroid resistant nephrotic syndrome is ≥512 with area under curve 0.992, sensitivity 96.3%, specificity 88.9%, positive predictive value 89.7%, negative predictive value 96%, and overall accuracy 92.6%. Our study revealed that, there is non-significant correlation between urinary monocyte chemotactic protein 1 among patients with NS and either age, age of disease onset and disease duration. In our study, there is statistically significant positive correlation between urinary monocyte chemotactic protein 1 among patients with NS and all of depth of proteinuria, PCR, duration of steroid use and serum cholesterol. There is statistically significant negative correlation between urinary monocyte chemotactic protein 1 among patients with NS and serum albumin. Conclusion: Urinary MCP-1 can be a useful biomarker for diagnosing and monitoring pediatric patients with idiopathic nephrotic syndrome. The study found also a positive correlation between urinary MCP-1 levels and the depth of proteinuria, PCR, duration of steroid use, and serum cholesterol, while there was a negative correlation with serum albumin.

KeyWords: Urinary and Plasma Monocyte Chemotactic Protein 1 - Steroid Responsiveness – Idiopathic Nephrotic Syndrome.

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Introduction.

Nephrotic syndrome is defined as hypoalbuminemia, edema, and proteinuria (24 hour urine protein > 40 mg/m2 /hr or urinary protein to creatinine ratio > 2000 mg/gm or protein > 300 mg/dL or 3+ on urine dipstick. Nephrotic syndrome is a frequent pediatric kidney disorder that affects 2– 16 per 100,000

children each year. It can occur at any age during childhood and adolescence (**1**).

Steroid-sensitive nephrotic syndrome (SSNS) is described as remission within the initial four weeks of corticosteroid therapy (**2**). The failure to achieve complete remission after eight weeks of corticosteroid therapy is described as steroidresistance nephrotic syndrome (SRNS)(**2**).

Althoughthe pathogenesis and pathophysiology of idiopathic nephrotic syndrome (INS) are unknown, it has been suggested that the immune system plays an important role. A link between several cytokines and chemokines and INS has been reported. Histological reports suggest that macrophages play an important role in the pathogenesis of focal segmental glomerulosclerosis (FSGS), a form of steroid-resistant nephrotic syndrome(**3).**

Monocyte chemotactic protein-1 (MCP-1) belongs to the CC-chemokine family, is encoded on chromosome 17, and is composed of 76 amino acids. It is produced by mesangial, tubular, and epithelial cells in the kidney, as well as smooth muscle cells. It is mainly expressed by monocytes, activated macrophages, T cells, and natural killer cells (**4**). MCP-1 causes monocyte migration and retention, as well as fibroblast transformation, in the glomeruli, and hence plays a significant role in glomerular inflammation. The pathophysiology of renal glomerular and tubular injury was linked to urinary MCP-1(**5).**

The objectives of this study were to investigate the diagnostic value of plasma and urinary MCP-1 in pediatric patient with idiopathic nephrotic syndrome, to detect effect of disease remission and activity on these levels and to compare our results between case of age and sex matched control group.

Patients and Methods

A-Technical design:

Setting:

Pediatrics nephrology unit, pediatric nephrology outpatient clinic at Zagazig university hospitals.

Population or Subjects:

Children attending at pediatric inpatient and outpatient clinic. They were classified into:

- **Group A:** This group included 27 nephrotic patients in remission (marked reduction in proteinuria to < 4 mg/m^2/hr or urine albumin dipstick of 0 to trace for 3 successive days in association with resolution of edema) **(2).**
- **Group B:** This group included 27 nephrotic patients in activity either with 1st attack or relapsers (severe proteinuria > 40 mg/m^2/hr or urine albumin dipstick ++ or more on 3 successive days, often with association or recurrence of edema) after withdrawal of steroid therapy **(3).**
- **Control group:** This group included 27 age and sex matched healthy children attending general pediatric clinic.

Sample size:

Assuming the mean urinary MCP1 was 100+ 85 vs 180+ 170 in SSNS vs SRNS group.At 80% power and 95 % CI, the estimated sample was 81 subject, 27 subject in each group. Open epi

Inclusion criteria:

- Approval to participate in the study.
- Patients with idiopathic nephrotic syndrome .
- Both sex.
- Children age from 2 years up to 16 years.

Exclusion criteria:

- Refusal to participate in the study.
- Patients with secondary nephrotic syndrome.
- Patients with any manifestations of systemic disease.
- Patients < 2 years or > 16 years.

B-OPERATIONAL DESIGN:

Study Design:

The study was a case control study.

Process:

All patients were subjected to the following:

Full history taking in the form of applied questionnaire including:

- Personal history: age, sex, residence.
- Onset, duration of illness.

Presenting symptoms:

Periorbital edema which is more apparent in the morning and decrease by the end of the day thenbecome generalized edema, fever, cough, dyspnea, nausea, vomiting, abdominal pain, frothy urine.

- Response to steroid therapy.
- Frequency of relapses.
- Complications of steroid therapy.
- Medication received.
- Outcome

Full clinical examination in the form of:

General examination including:

- Vital signs (temperature, respiratory rate, heart rate, blood pressure & its centile).
- Anthropometric measurements (weight, height).

Local examination including:

- Abdominal examination.
- Chest examination.
- cardiac examination.
- Neurological examination.

Investigations:

All samples from all participants were submitted to the following:

Routine lab investigations including:

- Complete blood count (CBC), C – reactive protein (CRP), serum creatinine, blood urea, serum albumin, serum total cholesterol, complete urine analysis and urine protein/creatinine ratio.

Specific tests:

- Plasma and urinary monocyte chemotactic protein-1 (MCP-1) was done by ELISA technique.
- Data were analyzed statistically.
- Preparing conclusions and recommendations.

Urine Sampling

Random midstream urine samples were taken from patients and controls in clean containers at about 10 am, and divided into two portions: the first portion for complete urine analysis, urinary protein/creatinine ratio, the second portion was collected in sterile tube and centrifuged at 1000 RPM for 20 minutes. The supernatant was then collected, aliquoted and immediately frozen at -20°C till the time of assessment of MCP-1 using a commercially available ELISA kit supplied by Elabscience, Inc, USA, catalog number: E-EL-H6005, sensitivity: 37.5pg/mL, and detection range: 62.5-4000pg/mL.

STATISTICAL ANALYSIS

Data was collected, coded then entered as a spread sheet using Microsoft Excel 2016 for Windows, of the Microsoft Office bundle; 2016 of Microsoft Corporation, United States. Data was analyzed using IBM Statistical Package for Social Sciences software (SPSS), (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). The Kolmogorov-Smirnov test was used to verify the normality of distribution. Continuous data was expressed as mean ± standard deviation, median & IQR while categorical data as numbers and percentage. A statistical value <0.05 was considered as significant.

- **Analytic statistics:**
- **Chi-square test**; used to study the association between two qualitative variables.
- **Analysis of variance (ANOVA or F test**): was used for continuous data to test for significant difference between more than two normally distributed groups. Assumptions of normality in each group and homogeneity of variances were verified using Shapiro-Wilk test and Levine's test, respectively.
- **Kruskal-Wallis test**: It is a non-parametric equivalent to ANOVA and used when ANOVA assumptions were violated to compare between more than two groups of skewed data.
- **Post Hoc tests**: Tukey honestly significant difference (Tukey- HSD) test was used as a post hoc test to adjust for multiple comparisons after significant ANOVA test to indicate which significant difference between pairs of groups whereas Bonferroni post hoc test was used after significant Kruskal- Wallis test.

-Correlation analysis (using Spearman/Pearson's method): To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength and direction of the linear relationship between two variables.

-Logistic Regression: To measures the relationship between the categorical target variable and one or more independent variables. It is useful for situations in which the outcome for a target variable can have only two possible types

-The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the Sensitivity and specificity for quantitative Diagnostic measures that categorize cases into one of two groups.

Results

Group A: Nephrotic disease in remission, Group B: Nephrotic disease in activity, Group C: Healthy control group

Table (1) Comparison between the studied groups regarding demographic data and presentation of the disease:

	Group A N=27 (%)	Group B N=27 (%)	Group C N=27 (%)	χ^2	p
Sex:					
Female	15 (55.6%)	12 (44.4%)	12 (44.4%)	0.89	0.641
Male	12 (44.4%)	15 (55.6%)	15 (55.6%)		
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**F**	**p**
Age (year)	7.27 ± 1.81	7.54 ± 1.65	6.74 ± 1.81	1.435	0.244
	Median (IQR)	**Median (IQR)**		**Z**	**p**
Age of onset (year)	3.6(2.7 – 4.1)	4.1(3.4 – 4.5)		-1.923	0.055
Disease duration (year)	4.15(2.58 – 4.95)	3.85(2.63 – 4.93)		-0.412	0.68

χ^2Chi square test F One way ANOVA test Z Mann Whitney test

There is statistically non-significant difference between the studied groups regrading age, age of onset, disease duration or gender

Table (2) Comparison between the studied groups regarding symptoms and complication of therapy

	Group A N=27 (%)	Group B N=27 (%)	χ^2	p
Renal failure				
Absent	27 (100%)	25 (92.6%)	Fisher	0.491
Present	0 (0%)	2 (7.4%)		
Thrombosis (no)	0 (0%)	0 (0%)	0	>0.999
Infection:				
No infection	24 (88.9%)	22 (81.5%)		
Chest infection	1 (3.7%)	2 (7.4%)	MC	>0.999
Pyuria	2 (7.4%)	3 (11.1%)		
Complications of steroid				
Therapy				
Gastritis	26 (96.3%)	25 (92.6%)	Fisher	>0.999
Hypertension	3 (11.1%)	4 (16%)	Fisher	0.698
Obesity	1 (3.7%)	1 (3.7%)	0	>0.999
Growth retardation	0 (0%)	1 (3.7%)	Fisher	>0.999
Striarubra	0 (0%)	1 (3.7%)	Fisher	>0.999
Multiple fracture	0 (0%)	1 (3.7%)	Fisher	>0.999

**p≤0.001 is statistically highly significant χ^2Chi square test MC Monte Carlo test

There is statistically non-significant difference between the studied nephrotic patients regarding incidence of complications of therapy, thrombosis, renal failure or infection

Table (3) Comparison between the studied groups regarding therapy

	Group A N=27 (%)	Group B N=27 (%)	χ^2	P
Immune suppressive				
Steroid	27 (100%)	27 (100%)	0	>0.999
MMF	3 (11.1%)	25 (92.6%)	Fisher	<0.001**
Supportive				
PPI	26 (96.3%)	26 (96.3%)	0	>0.999
Calcium	24 (88.9%)	24 (88.9%)	0	>0.999
Vitamin D3	26 (96.3%)	27 (100%)	Fisher	>0.999
ACEI	27 (100%)	27 (100%)	0	>0.999
Antihypertensive:				
No	24 (88.8%)	23 (85.1%)		
Amlodipine	3 (11.1%)	4 (14.8%)	Fisher	>0.999

χ^2Chi square test MC Monte Carlo test

There is statistically significant difference between the studied nephrotic patients regarding use of MMF
There is statistically non-significant difference between the studied nephrotic patients regarding use of steroid, supportive or antihypertensive therapy.

Table (4) Comparison between the studied groups regarding kidney function test:

	Group A N=27 (%)	Group B N=27 (%)	Group C N=27 (%)	F	p
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Creatinine (mg/dl)	0.42 ± 0.14	0.44 ± 0.12	0.44 ± 0.16	0.296	0.7452
Urea (mg/dl)	24.32 ± 1.26	24.04 ± 1.07	23.66 ± 2.61	0.926	0.401

F One way ANOVA test

There is statistically non-significant difference between the studied groups regrading serum urea or creatinine.

Table (5) Comparison between the studied groups regarding Protien/creatine ratio and urine analysis:

	Group A N=27 (%)	Group B N=27 (%)	Group C N=27 (%)	F	p
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Protein/creatinine ratio	511.37 ± 102.07	6185.09 ± 1895.19	38.81 ± 7.86	263.054	<0.001**
LSD	P_1<0.001**	P_2<0.001**	P_3 0.117		
Urine analysis(dip stick)				χ^2	
Negative	22 (81.5%)	0 (0%)			
Trace	5 (18.5%)	0 (0%)		46.202	<0.001**
2+	0 (0%)	13 (48.1%)			
3+	0 (0%)	14 (51.9%)			

F One way ANOVA test LSD Fisher least significant difference **p≤0.001 is statistically highly significant *p<0.05 is statistically significant p1 difference between groups A and B p2 difference between groups B and C p3 difference between groups A and C χ^2Chi square for trend test

There is statistically **significant** difference between the studied nephrotic patients regarding urine analysis (dip stick) (81.5% within steroid sensitive had no albuminuria while 51.9% within steroid resistant groups had proteinuria +3). There is statistically **significant** difference between the studied groups regrading protein/creatinine ratio (on doing posthoc test, the difference is **significant** between steroid-resistant group and each other group).

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Table (6) Comparison between the studied groups regarding laboratory data:

	Group A N=27 (%)	Group B N=27 (%)	Group C N=27 (%)	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Albumin (g/dl)	3.21 ± 0.37	2.47 ± 0.62	4.22 ± 0.32	100.35	<0.001**
LSD	P_1<0.001**	P_2<0.001**	P_3<0.001**		
Cholesterol (mg/dl)	143.63 ± 20.17	196.04 ± 19.26	94.0 ± 13.34	220.69	<0.001**
LSD	P_1<0.001**	P_2 0.001**	P_3<0.001**		
Platelet (10^3/mm^3)	230.11 ± 54.64	227.56 ± 67.96	222.48 ± 54.55	0.115	0.891
WBCs (10^3/mm^3)	7.84 ± 1.28	7.84 ± 1.29	8.34 ± 1.11	1.487	0.232
Hemoglobin (g/dl)	11.15± 0.9	11.14 ± 073	11.05 ± 1.17	0.093	0.911

F One way ANOVA test LSD Fisher least significant difference **p≤0.001 is statistically highly significant *p<0.05 is statistically significant p1 difference between groups A and B p2 difference between groups B and C p3 difference between groups A and C

There is statistically **significant** difference between the studied groups regrading both serum albumin and total cholesterol (on doing posthoc test, the difference is significant between each two individual groups) There is statistically non-significant difference between the studied groups regrading hemoglobin, white blood cells, or platelet count

Table (7) Comparison between the studied groups regarding Urinary and Plasma Monocyte Chemotactic Protein 1:

Monocyte Chemotactic Protein 1(pg/ml)	Group A N=27 (%)	Group B N=27 (%)	Group C N=27 (%)	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Plasma level	60.96 ± 17.97	62.07 ± 15.44	68.7 ± 17.21	1.655	0.198
Urinary level	401.59 ± 83.53	785.37 ± 110.95	56.93 ± 11.7	553.699	<0.001**
LSD	**P_1<0.001****	**P_2<0.001****	**P_3<0.001****		

F One way ANOVA test LSD Fisher least significant difference **p≤0.001 is statistically highly significant *p<0.05 is statistically significant p1 difference between groups A and B p2 difference between groups B and C p3 difference between groups A and C

There is statistically **significant** difference between the studied groups regrading **Urinary Monocyte Chemotactic Protein 1** (on doing posthoc test, the difference is significant between each two individual groups). There is statistically non-significant difference between the studied groups regrading **plasma Monocyte Chemotactic Protein 1**

Table (8) Performance of Urinary Monocyte Chemotactic Protein 1 in diagnosis of nephrotic syndrome

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
≥79	1	100%	96.3%	98.2%	100%	98.8%	<0.001**

**p≤0.001 is statistically highly significant PPV positive predictive value NPV negative predictive value AUC area under curve

The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of nephrotic syndrome is ≥79 with area under curve 1, sensitivity 100%, specificity 96.3%, positive predictive value 98.2%, negative predictive value 100%, and overall accuracy 98.8%

Table (9) Comparison between the studied groups regarding relapse

	Group A N=27 (%)	Group B N=27 (%)	χ^2	p
Relapse				
First attack	1 (3.7%)	1 (3.7%)		
Infrequent relapser	23 (85.2%)	21 (77.8%)	0.294	0.587
Frequent relapse	3 (11.1%)	5 (18.5%)		

χ^2Chi square for trend test

There is statistically non-**significant** difference between the studied nephrotic patients regarding relapse

Table (10) Performance of Urinary Monocyte Chemotactic Protein 1 in diagnosis of steroid-resistant nephrotic syndrome

Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
≥512	0.992	96.3%	88.9%	89.7%	96%	92.6%	<0.001**

**p≤0.001 is statistically highly significant PPV positive predictive value NPV negative predictive value AUC area under curve

The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of steroid resistant nephrotic syndrome is ≥512 with area under curve 0.992, sensitivity 96.3%, specificity 88.9%, positive predictive value 89.7%, negative predictive value 96%, and overall accuracy 92.6%

Table (11) Correlation between plasma monocyte chemotactic protein 1 and the studied parameters among patients with nephrotic syndrome:

	r	P
Age (year)	-0.132	0.341
Age at onset (year)	-0.043§	0.76
Disease duration (year)	-0.044§	0.754
Proteinuria	0.079	0.569
Creatinine (mg/dl)	0.104	0.452
Protein/creatinine ratio	0.048	0.732
Urea (mg/dl)	0.003	0.979
Albumin (g/dl)	0.003	0.984
Cholesterol (mg/dl)	0.104	0.452
Platelet (10^3/mm^3)	-0.164	0.237
WBCs (10^3/mm^3)	-0.119	0.393
Relapse	-0.021§	0.881
Steroid duration	0.027§	0.848

r Pearson correlation coefficient §Spearman rank correlation coefficient *p<0.05 is statistically significant

There is non-significant correlation between plasma monocyte chemotactic protein 1 among patients with NS and either age, age of disease onset, disease duration, duration of steroid use, WBCs, platelet, PCR, urea, creatinine, proteinuria, serum albumin, cholesterol, frequency of relapse

Table (12) Correlation between urinary monocyte chemotactic protein 1 and the studied parameters among patients with nephrotic syndrome:

	r	P
Age (year)	0.128	0.358
Age at onset (year)	0.214	0.12
Disease duration (year)	-0.001	0.997
Proteinuria	0.793	**<0.001****
Creatinine (mg/dl)	0.085	0.541
Protein/creatinine ratio	0.789	**<0.001****
Urea (mg/dl)	-0.054	0.635
Albumin (g/dl)	-0.441	**<0.001****
Cholesterol (mg/dl)	0.733	**<0.001****
Platelet (10^3/mm^3)	-0.117	0.4
WBCs (10^3/mm^3)	0.096	0.49
Hemoglobin (g/dl)	0.028	0.838
Relapse	0.12	0.388
Steroid duration	0.758	**<0.001****

r Pearson correlation coefficient §Spearman rank correlation coefficient *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

There is statistically significant positive correlation between urinary monocyte chemotactic protein 1 among patients with NS and all of depth of proteinuria, PCR, duration of steroid use and serum cholesterol. There is statistically significant negative correlation between urinary monocyte chemotactic protein 1 among patients with NS and serum albuminon the other hand, there is non-significant correlation between urinary monocyte chemotactic protein 1 among patients with NS and either age, age of disease onset, disease duration, WBCs, hemoglobin, platelet, urea, creatinine.

Table (13) Linear regression analysis of factors associated with urinary monocyte chemotactic protein 1 among patients with nephrotic syndrome

	Unstandardized Coefficients		Standardized Coefficients	t	p	95% Confidence Interval	
	B	Std. Error	Beta			Lower	Upper
(Constant)	93.711	114.014		.822	0.415	-135.182	322.604
Protein/creatinine ratio	0.037	0.008	0.545	4.663	<0.001*	0.021	0.054
Cholesterol	2.205	0.770	0.335	2.862	0.006*	0.658	3.752

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant

Among factors significantly correlated to urinary monocytes chemotactic protein-1, protein creatinine ratio (unstandardized β=0.037, p<0.001), and cholesterol unstandardized β=2.205, p=0.006), independently significantly associated with it

Discussion

The current study showed that, there is statistically non-significant difference between the studied groups regrading hemoglobin, white blood cells, or platelet count.

This is in harmony with **El hamshary et al. (6**) who reported that, there was no statistically significant difference between patients and control group as regard CBC.

In our study, there is statistically non-significant difference between the studied groups regarding serum urea or creatinine.

Our study agrees with **Souto et al., (7)** who reported that no differences were detected, in nitrogen waste levels (serum creatinine and blood urea), between INS groups and controls.

This is in agreement with **Amin et al., (8)** who found that there is no statistically significant difference between patient group (children with idiopathic nephrotic syndrome) and control group as regards blood urea and serum creatinine.

In this study, there is statistically **significant** difference between the studied groups regarding both serum albumin and total cholesterol (on doing posthoc test, the difference is significant between each two individual groups)

In their multivariate analysis **AbdelMassih et al. (9**) showed that serum cholesterol failed to be a statistically significant predictor of either systolic or diastolic dysfunction in NS (**10**). 4418

In our study, there is statistically **significant** difference between the studied groups regarding **Urinary Monocyte Chemotactic Protein 1** (on doing posthoc test, the difference is significant between each two individual groups).

This is in accordance with **Abdel Haie et al. (11)** who found that urine MCP-1 was higher in children with INS, implying that immune cells are involved in the development of NS. MCP-1 levels in the urine were substantially higher during relapse than during remission. MCP-1 causes monocyte migration and retention, as well as fibroblast transformation, in the glomeruli, and hence plays a significant role in glomerular inflammation.

A recent Japanese investigation studied cytokines in plasma and urine samples from 18 patients with NS, at onset and after therapy, and identified MCP-1 to be elevated in SRNS after therapy **(3).**

A recent study investigated the effect of the MCP-1 2518 A/G polymorphism on the incidence and clinical course of biopsy-proven focal segmental glomerulosclerosis in children and found that the AA genotype might be a risk factor for disease progression (**12).** Moreover, these authors found that urinary levels of MCP-1 were significantly higher in focal segmental glomerulosclerosis versus SSNS and healthy controls, although serum levels of MCP-1 were comparable between these groups**.**

The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of nephrotic syndrome is ≥79 with area under curve 1, sensitivity 100%, specificity 96.3%, positive predictive value 98.2%, negative predictive value 100%, and overall accuracy 98.8%.

Wasilewska et al. (13) reported that, the level of uMCP-1/cr did not differ between children with a first or second INS attack and children with multiple relapses ($p > 0.05$).

The best cutoff of urinary monocyte chemotactic protein 1 in diagnosis of steroid resistant nephrotic syndrome is ≥512 with area under curve 0.992, sensitivity 96.3%, specificity 88.9%, positive predictive value 89.7%, negative predictive value 96%, and overall accuracy 92.6%.

In another study, **Khatibi et al., (14**) showed a higher level of uMCP-1 in SRNS patients compared to SSNS patients, indicating that uMCP-1 can predict glucocorticoid resistance.

In our study, there is statistically significant positive correlation between urinary monocyte chemotactic protein 1 among patients with NS and all of depth of proteinuria, protein creatinine ratio, duration of steroid use and serum cholesterol. There is statistically significant negative correlation between urinary monocyte chemotactic protein 1 among patients with NS and serum albumin

This agrees with **Abdel Haie et al. (12)** who found significant negative correlation between uMCP, and serum albumin, and also significant positive correlations between uMCP and serum cholesterol, and UPCR, which indicate that uMCP may be considered a sensitive biomarker of disease activity.

Moreover, many studies observed that patients with active idiopathic nephrotic syndrome had considerably higher urine MCP-1 excretion than patients in remission or controls(**14, 15).**

Conclusion:

Urinary MCP-1 can be a useful biomarker for diagnosing and monitoring pediatric patients with idiopathic nephrotic syndrome. The study found also a positive correlation between urinary MCP-1 levels and the depth of proteinuria, protiene creatinine ratio, duration of steroid use, and serum cholesterol, while there was a negative correlation with serum albumin.

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