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Research Article

A Cross-Sectional Study of Urinary Neutrophil Gelatinase-Associated Lipocalin and its Association with Steroid Responsiveness in Iraqi Children with Idiopathic Nephrotic Syndrome

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Abstract

Background: Steroid-resistant nephrotic syndrome (SRNS)is associated with serious complications and financial burdens. Studies reported increased levels of urinary neutrophil gelatinase-associated lipocalin (uNGAL) in children with idiopathic nephrotic syndrome (INS).

Objectives: This study aimed to evaluate the uNGAL potential to distinguish SRNS from steroid-sensitive nephrotic syndrome (SSNS) in Iraqi children.

Methods: Children with SRNS (n=31) and SSNS (n=32) were recruited from Babylon Hospital for Maternity and Pediatrics from 29March to 22June 2022. Patients' collected data included demographics, clinical characteristics, and urinary lab tests. The uNGAL concentrations were measured via a commercially available ELISA kit.

Results: A significantly higher uNGAL median (p-value<0.001) was noted in the SRNS group (median [IQR] = 131.512 [30.28] ng/mL) than in the SSNS group (88.45 [41.6] ng/mL). The correlation between uNGAL levels and estimated glomerular filtration rate (eGFR) was negative (Spearman's rho coefficient = − 0.599, p<0.001). The discriminatory power ofuNGAL to discern SRNS from SSNS was significantly high (AUC=0.899, p<0.0001) with a sensitivity of 87.1% and specificity of 87.5% at an optimal cut-off value of 111.091 ng/mL.

Conclusion: uNGAL is associated with a reliable discriminatory strength to distinguish, noninvasively, children with SRNS from those with SSNS.

Keywords: Biomarker; Steroid-resistant nephrotic syndrome; Neutrophil gelatinase-associated lipocalin; Steroid-sensitive nephrotic syndrome.

Introduction

One of the glomerular diseases in children, nephrotic syndrome (NS) is the most common condition, which is predominately idiopathic in etiology. Development of episodic events of relapses that involve edema, proteinuria, and hypoalbuminemia are the distinguishing features of NS(1). Minimal-change disease (MCD) and focal segmental glomerulosclerosis (FSGS) are the two most frequently encountered histological types of the disease upon studying renal biopsy(2–5). Steroid-resistant nephrotic syndrome (SRNS) was associated with a higher risk of disease progression and complication development as compared to steroid-sensitive nephrotic syndrome (SSNS)(6–8). An ongoing escalation in the number of SRNS cases has been noted and was attributed to the rise in the emerging cases of FSGS in children worldwide (including in Iraq)(9–12). This is concerning as
FSGS is the most common non-genetic cause ofend-stage renal disease (ESRD) and chronic renal failure during childhood and is associated with a high recurrence rate following transplantation(13–16).

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It is the standard of care for patients with idiopathic nephrotic syndrome (INS) to go through a trial of a high-dose steroid regimen (for a prolonged period of up to three months), which is considered both a therapeutic and diagnostic intervention. The patient is presumed SRNSif remission is not acquired, and the histopathological category is confirmed with a biopsy study(17,18).

It has been reported that diagnosis of SRNS (more specifically FSGS) is often missed with a single pediatric needle biopsy because of the limited number of biopsied glomeruli and the focally localized patterns of the glomerular lesions. Subsequently, an accurate diagnosis of FSGS requires conducting several biopsies(19).

The absence of validated diagnostic markers that specify SRNS from SSNS in clinical practice, where a "one-size fits all" approach is routinely adopted, creates a dire need for a biomarker test (preferably a non-invasive one) to help in the identification of SRNS.The availability of a test that offers further insight into the likely responsiveness of a patient to a particular regimen can aid the physicians to tailor the therapeutic plan for the better care of that patient. The management strategy can be significantly improved by prompting the earlier

initiation of immunosuppressant alternatives and preventing unnecessary exposure to long-term high-dose steroid regimens(20).

In patients with ISN, damage to the glomerular barrier and the tubular cubulin/megalin-mediated endocytosis have been proposed to increase the levels of uNGAL(21).In a cohort of 96 chronic kidney disease (CKD) patients (stages 2-4) that were prospectively followed over three months, Bolignano et al. highlighted that the initial uNGAL concentrations were significantly higher in patients with progressive CKD than those of non-progressive CKD.uNGAL was still independently capable of predicting CKD progression even after adjusting for other predictors such as age and kidney impairment severity(22).

It has been hypothesized that the uNGAL levels have a differentiating ability for children with SRNS from SSNS because SRNS is associated with a higher risk of disease progression and poor prognosis when compared to SSNS.In India and the United States, the uNGAL levels were significantly higher in SRNS as compared to SSNS(23,24). However, another study from Europe did not find a statistically significant difference in the uNGAL concentrations among children with SRNS compared to those with SSNS (p-value>0.05)(25).

With these inconsistent observations among different populations in mind, more investigations are still necessary to provide additional information about the capability of uNGAL to predict steroid responsiveness in children with INS, especially in Iraq where, to our knowledge, the literature is lacking such investigations. Thus, we performed this study to assess the ability of uNGAL as a non-invasive biomarker to differentiate SRNS from SSNS in Iraqi children.

Patients and Methods:

Settings and study design: This is a cross-sectional study conducted in the department of Pediatrics at Babylon Hospital for Maternity and Pediatrics from March to June 2022. The Human Research Committee of Babylon Directorate of Health (Decision number: 44 on 28/3/2022) and the Research Ethics Committee at the University of Baghdad -College of Pharmacy (Approval No.: RECAUBCP17102021A on 17/10/2021) approved the study protocol.Informed consent was obtained from all study participants (or parents/caregivers) before their enrollment in the study.

Participants: Patients aged 1-14 years who were already diagnosedwith steroid-sensitive or steroid-resistant INS were recruited from the pediatric nephrology consultation clinic from 29March to 22June 2022.Children who were categorized as steroid-sensitive were those responsive within the first four weeks of daily prednisolone therapy (2 mg/kg/day or 60 mg/m^{2}and a maximum daily dose of 60 mg/day) as evidenced by the lack of proteinuria on early morning urine dipsticks (less than 1+). Alternatively, the steroid-resistant group included children who did not acquire remission (<1+ proteinuria on early morning urine dipsticks) after either eight weeks of daily prednisolone or four to six weeks of daily prednisolone regimen (2 mg/kg/day or 60 mg/m^2 and a maximum daily dose of 60 mg/day) followed by another four to six weeks of alternate day prednisolone regimen (1.5 mg/kg/day or 40 mg/m^2 and a maximum daily dose of 50 mg/day)(17,18,26).

Patients with fever, gross hematuria, acute kidney injury, active or recurrent urinary tract infection, and NS secondary to systemic diseases such as lupus nephritis, viral infections, or diabetes were excluded. The patients visited the clinic for routine follow-up and were recruited consecutively after their consent and satisfaction with the study inclusion and exclusion criteria.

Sample size estimation: The sample size was calculated using an online calculator (https://sample-size.net/sample-size-ci-for-auroc/) (27). The values of the expected area under the ROC curve and the width of the confidence interval (0.90 and 0.16, respectively) were based on the results of previous studies(23,24). The calculated sample size was 63 when the proportion of the sample having the positive studied outcome (steroid resistance) is 50% of the sample. Thus, 31 patients were included in the positive outcome group (steroid resistant) and 32 patients were recruited for the negative outcome group (steroid sensitive).

Data collection: Data about the clinical and demographic characteristics of all the study participants were collected in a predetermined sheet at the time of enrollment. Demographics and clinical data included gender, age, height, weight, blood pressure, age at onset, intake of concomitant medications, urinalysis, proteinuria (by urine dipstick), serum urea, serum creatinine, serum albumin, steroid-response history, and immunosuppressant/drug intake were recorded forall the study participants. The updated Schwartz equation was used to calculate the estimated glomerular filtration rate (eGFR) based on the participant's height and serum creatinine.Additionally, all patients were screened for autoantibodies (anti-double stranded DNA antibodies and anti-nucleic acid antibodies), serum complement C3 levels (to exclude NS secondary to autoimmune diseases such as systemic lupus erythematosus), serum fasting blood glucose (to exclude diabetes mellitus), and viral antibodies to HIV, HBV, and HCV (to exclude NS secondary to viral infections). Measurement of uNGAL levels was conducted using acommercially available ELISA kit (Bioassay Technology Laboratories, Zhejiang, China). Urine collection was performed as part of a routine clinic visit. After collection, the urine sample was subjected to centrifugation at 3000 RPM for 20 minutes, aliquoted, and stored at -80 °C. Repeated freeze-thaw cycles of more than two times were not allowed.

Statistical analysis:

The statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) statistics software (version 22). Categorical data for the demographic and clinical characteristics of the study subjects were presented by frequencies and percentages and the Chi-square test was used to test for the association between categorical variables.

Shapiro-Wilk test was used to assess the distribution normality of the continuous data. The normally distributed variables were presented using mean and standard deviation. The median and interquartile range were used to describe the variables with non-normal data. The normal data of both study groups (height, serum albumin, and eGFR) were compared using the unpaired t-test. We used the Mann-Whitney U test to compare the non-normal data.

Subgroup analysis was conducted among children with SSNS to examine the influence of proteinuria presence on the uNGAL levels. Additionally, SRNS patients with concomitant use of calcineurin inhibitors (CNIs) were compared with those without CNI therapy to test whether CNI intake could have influenced uNGAL levels in children with INS. The receiver operator characteristics (ROC) curve was analyzed to determine the discriminatory power of uNGAL level to distinguish SR patients from SS patients.

Spearman rank correlation analysis was performed to evaluate the correlation between the uNGAL levels with the renal function of the studied NSpatients, which was represented by eGFR.A statistically significant finding was considered when the p-value was less than 0.05.

Results

Demographics:

At enrollment, the two groups of children included in this study had comparable ages, disease duration, gender, weightand height, table (1).

Table (1): Demographiccharacteristics of the participants in the two study groups

Demographiccharacteristics	The study participants (n=63)		p-value
	SSNS (n=32)	SRNS (n=31)	
Age at enrollment [years; median (IQR)]	6.48 (3.4)	8.5 (6)	0.104[§]
Gender [male; frequency (%)]	20 (62.5)	21 (67.7)	0.432
Age at onset of disease [years; median (IQR)]	4 (2)	3 (5.5)	0.19[§]
Weight [Kg; median (IQR)]	21 (10.6)	25 (25)	0.132[§]
Height (cm; mean ± SD)	111.81 ± 17.14	118.77 ± 26.09	0.218[ǂ]

[§] Significance value for Mann-Whitney U test. [ǂ] Significance value for independent samples t-test.

Subjects with SRNS had significantly higher serum creatinine and blood urea levels as well as lower eGFR values as compared to SSNS ($p<0.05$), table 2.

Table (2): Biochemical characteristics of the two groups of the study participants

Biochemical characteristic	The study participants (n=63)		p-value
	SSNS (n=32)	SRNS (n=31)	
Serum albumin (gm/L; mean ± SD)	37.9 ± 7.15	32.4± 11.29	0.024[ǂ]
Serum creatinine [µmol/L; median (IQR)]	54 (22.8)	65 (32.0)	0.007[§]
Blood urea [mmol/L; median (IQR)]	2.8 (1.45)	4.1 (2.8)	0.003[§]
eGFR (mL/min/1.73 m^2; mean ± SD)	72.9 ± 14.71	63.6 ± 14.31	0.014[ǂ]

[§] Significance value for Mann-Whitney U test. [ǂ] Significance value for independent samples t-test.

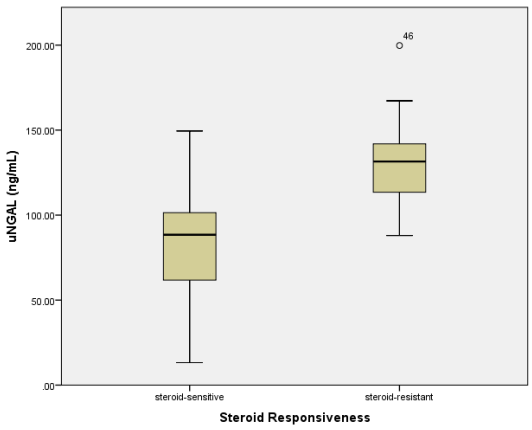
A concomitant intake of angiotensin-converting enzyme inhibitors (ACEIs; n=8) and diuretics (n=14) was more frequent in SRNS than in SSNS (n= 2 and 5, respectively) (see table 3).

Table (3): Clinical characteristics of the study participants in the two groups

Clinical characteristics	The study participants (n=63)		p-value
	SSNS (n=32)	SRNS (n=31)	
Presence of hypertension (frequency, %)			
Systolic blood pressure >95 percentile	4 (12.5)	5 (16.1)	0.479*
Diastolic blood pressure >95 percentile	3 (9.4)	7 (22.6)	0.138*
Pathology upon biopsy (frequency, %)			
Focal segmental glomerular sclerosis	-	1 (3.2)	NA
Membranoproliferative glomerulonephritis	-	1 (3.2)	NA
Minimal change disease	-	3 (9.7)	NA
No biopsy	32 (100)	26 (83.9)	NA
Immunosuppressant regimen (frequency, %)			
Prednisolone	32 (100)	3 (9.7)	NA
Prednisolone and cyclosporine	0	18 (58.1)	NA
Prednisolone and tacrolimus	0	3 (9.7)	NA
Prednisolone and chlorambucil	0	1 (3.2)	NA
Prednisolone and mycophenolate mofetil	0	6 (19.4)	NA
Concomitant medications (frequency, %)			
ACEI	2 (6.3)	8 (25.8)	0.036*
Statin	2 (6.3)	6 (19.4)	0.118*
Diuretic	5 (15.6)	14 (45.2)	0.011

* Significance value for Fisher's Exact Test. Statistically significant p-values are in bold.

Quantitative analysis of uNGAL levels: Children with SRNS showed significantly higher uNGAL levels in comparison to those with SSNS (median [IQR] = 131.512 [30.28] vs 88.45 [41.6] ng/mL; p-value<0.001), figure 1.



Figure(1): uNGAL levels in the studied groups (SSNS) and (SRNS)

Subgroup comparison analysis was conducted to test the possibility that the inclusion of patients without proteinuria had an impact on the uNGAL results of SSNS patients. The uNGAL levels of SSNS patients (n = 7) with proteinuria (median [IQR] = 80 [34.43]) were not significantly different from those (n = 25) without proteinuria (median [IQR] = 90.976 [46.91]; p-value>0.05), figure 2A. Regarding the SRNS group, there were 17 subjects with proteinuria and 14 subjects without proteinuria. Another subgroup analysis of the uNGAL levels was undertaken among SRNS patients and there was no statistically significant difference in the uNGAL levels of children who were treated with a calcineurin inhibitor (CNI) agent (median [IQR] = 129.52 [26.7]) as compared to those of children without concomitant CNI therapy (median [IQR] = 133.07 [49.49], p-value>0.05), figure 2B.

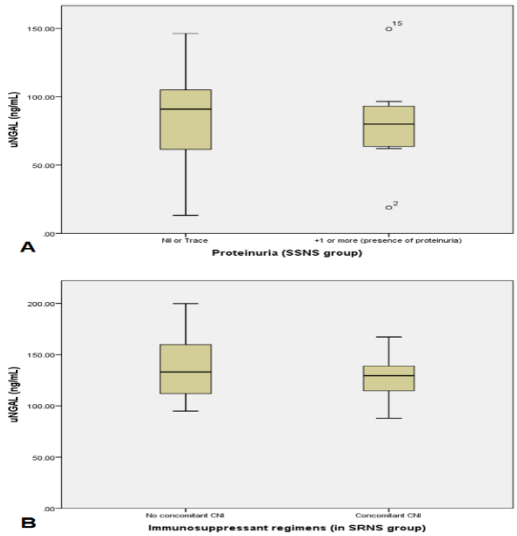


Figure (2): Subgroup analysis of uNGAL levels in children with SSNS and SRNS. A:uNGAL levels in SSNS subgroups with proteinuria and those without proteinuria.B:uNGAL levels in SRNS subgroups with CNI use and those without CNI use.

A statistically significant negative correlation was found between uNGAL levels and renal function in children with INS (Spearman's rho coefficient = −0.599, p<0.001). The decrease in eGFR measurements in the studied patients was associated with increasing uNGAL levels, figure 3. In SRNS, markedly elevated uNGAL levels were still noted in children with preserved renal function (eGFR>60 mL/min/1.73 m^2), figure 3B.

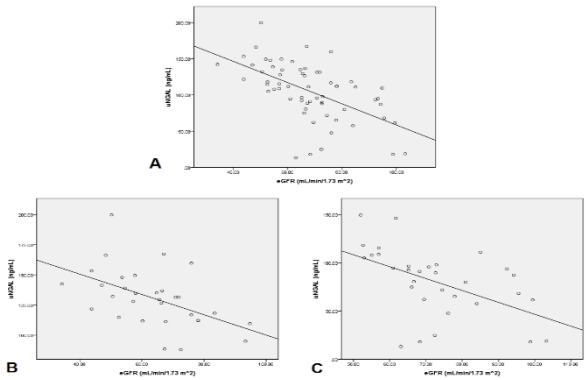
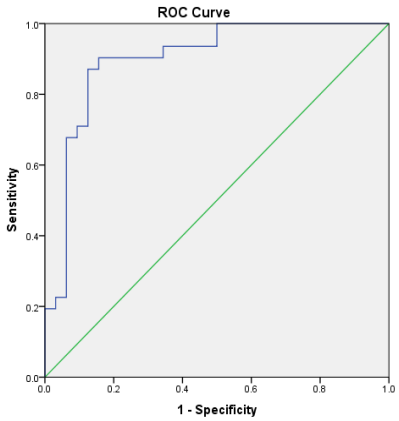


Figure (3): Correlation of uNGAL levels with renal function in children with INS (A: INS, n=63; B: SRNS, n=31; C: SSNS, n=32)

The ability of uNGAL to distinguish children with SRNS from SSNS was analyzed using the Receiver operator characteristic (ROC) curve. The findings revealed that the uNGAL level was an identifier parameter with a significantly reliable discriminatory power (AUC=0.899, p<0.0001). The ROC curve analysis of uNGAL levels also highlighted that a test sensitivity of 87.1% and specificity of 87.5% to discern children with SRNS from those with SSNS was produced with a cutoff value of 111.091 ng/mL (see figure 4 and table 4).



Figure(4): Receiver operator characteristic (ROC) curve analysis of uNGAL

Table (4): Results of the ROC curve analysis for uNGAL levels and the curve coordinates

Test result variable: Urinary neutrophil gelatinase-associated lipocalin (ng/mL)				
Area Under the Curve				
Area	Standard Error [a]	Asymptotic Significance [b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.899	0.041	<0.0001 (5.2017E-8)	0.818	0.980
Coordinates of the Curve				
Positive if Greater Than or Equal To [c]			Sensitivity	1 – Specificity
12.2000			1.000	1.000
15.6000			1.000	0.969
88.2450			0.968	0.500
106.4710			0.903	0.219
109.1770			0.903	0.156
110.2745			0.871	0.156
111.0910			0.871	0.125
112.0865			0.774	0.125
117.5240			0.677	0.094
133.3760			0.419	0.063
144.3015			0.226	0.063
147.0580			0.226	0.031
183.5030			0.032	0.000
200.7450			0.000	0.000
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				
c. The test result variable(s): uNGAL (ng/mL) has at least one tie between the positive actual state group and the negative actual state group. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.				

Discussion

Children with INSwhoare resistant to steroids are at a high risk of sustaining complications and progressing to end-stage kidney failure. Presently, there are no validated markers available for diagnostic purposes of SRNS. The routine approach to diagnosing SRNS is to observe the outcome of a trial of a long-term prednisolone course, which is typically followed by an invasive kidney biopsy for histopathological identification, and prediction of treatment responsiveness and disease progression(17,18).

This approach entails that individuals with SRNS are being exposed unnecessarily to high-dose steroid regimens as well as prompting the postponement of administering alternative and potentially more effective regimens.

uNGAL levels have been remarked as a strong predictor of chronic kidney disease (CKD) progression (22,28). This study aimed to assess whether uNGAL is capable of identifying children with SRNS who are more susceptible to poor prognosis and at a higher risk of progression to CKD than those with the more benign SSNS.

The results revealed that uNGAL measurements were significantly higher in patients with SRNS as compared to patients with SSNS. Moreover, it showed a high discriminatory power to distinguish patients with SRNS from patients with SSNS. This result is comparable to the findings of similar studies in the United States and India (23,24).

There were fewer patients without proteinuria (nil or trace upon early morning urine dipstick) in the SRNS group (n=14) as compared to the SSNS group (n=25) which implied a potential contribution to the higher levels of uNGALin the SRNS group and warranted further subgroup analysis. This subgroup analysis highlighted the lack of statistically significant differences in the levels of uNGAL among SSNS patients with proteinuria and those without proteinuria. Thus, the higher concentrations of uNGAL in the SRNS group are not fully attributed to the proteinuria status of the patients.

A "forest fire" theory has been suggested to explain the elevated levels of uNGAL with kidney injury where the rise in uNGAL was interpreted as a consequence of ongoing damage that triggers the surrounding "inflamed" cells to continuously produce NGAL(29).Increased concentrations of uNGALwere found to be a powerful predicting factor of disease progression and were significantly associated with histological findings of nephron fibrosis and atrophy in CKD patients (30).A possible interpretation of the higher uNGAL concentrations in the SRNS group is that children with SRNS who are at a higher risk of disease progression have an ongoing and more extensive underlying injury than children with SSNS, which is non-progressive.

Furthermore, this study found a negative correlation between the uNGAL measurements and renal function as evidenced by the increased levels of uNGAL that are associated with decreasing eGFR values, which was reported by another study(31).

In the current study, the eGFR values of the SRNS group were significantly lower as compared to those of the SSNS group. However, high levels of uNGAL were still present in SRNS subjects despite preserved renal function (eGFR>60 mL/min/1.73 m^2). This finding may reflect the ongoing and greater extent of kidney damage that is typically a part of SRNS pathology and a potential contributor to the higher levels of uNGAL in children with SRNS.

Moreover, Wasilewska et al showed that a CNI regimen was associated with an elevation in the concentration of uNGAL in children with NS. In the current study, a subgroup analysis was conducted among SRNS patients with and without CNI therapy, which revealed no statistically significant difference in the uNGAL levels inthe two subgroups. Interestingly, the probability that the greater increases inuNGAL level due to SRNS might have masked the small increases in uNGALlevel due to CNI therapy is still possible and merits further investigation(32).

Several urinary biomarkers have been evaluated for their ability to predict steroid responsiveness in children with NS(33–36). Khurana et al. revealed a characteristic urinary proteome that was able to specify steroid responsiveness via mass spectrometry technique (surface-enhanced laser desorption/ ionization). The latter study reported that a β-2 microglobulin fragment protein (11.117 KDa) was found in most of the SRNS patients but was absent in the SSNS group (33).

A later study used the same technology to explore urinary markers of steroid response in NS with an additional phase of finding validation using the Western blot technique. Piyaphanee et al discovered a fragment of α1-B glycoprotein (13.8 kDa) with a significantly high strength to classify SRNS from SSNS. However, this fragment was only detectable in 36.84% of the SRNS patients, particularly those with a greater decline in renal function(34). However, the unavailability of such mass spectrometry techniques in most laboratories and the anonymity of the identifier protein sequence limits the utility of these findings in clinical practice.

Other investigations assessed the responsiveness predicting capability of urinary cytokines in NS. Urinary TGF-beta (1) showed a promising potential to differentiate FSGS from MCD but a statistically significant difference in the marker expression was not found between SRNS and SSNS patients (35).

In Egypt, Ahmed et al studied the ability of urinary interleukin 8 to predict steroid resistance in children with NS. The authors compared the urinary IL-8 levels between SRNS and SSNS in two separate states of relapse and remission. Urinary IL-8 levels were significantly higher in the SRNS in the relapse group as compared to the SSNS in the relapse group and the SRNS in the remission group as compared to the SSNS in the remission group(36). Nevertheless, a statistically significant difference in the IL-8 levels was not found between the SSNS in the relapse group and the SRNS in the remission group(36).

There is an information gap in the literature regarding the potential of uNGAL as a noninvasive biomarker to distinguish SRNS from SSNS in Iraqi children with INS, which we attempted to cover through the findings of the current study. Before any conclusion can be drawn from this study, it is important to consider several limitations. This is a pilot cross-sectional study that derived the data from a small sample of patients who were attending a single center and on-ongoing steroid treatment at the time of recruitment.

A variability in the uNGAL data of the participants was noted in the SRNS group. Availability can inherently be encountered when investigating the treatment response in children with INS. Such

variability might be augmented in small samples. Nevertheless, we conducted a non-parametric statistical analysis, as the uNGAL data were not normally distributed. Furthermore, the groups were significantly different with such strength indicating that the analysis findings are indeed powerful.

It is also important to account for the probability that the rise in the uNGAL might originate from renal tubular damage, which could develop in various types of CKD rather than being a distinctively emerging event in patients with SRNS.

This preliminary work aims to build up baseline data and promote interest in future studies for appropriate validation of the utility of the initial uNGAL levels for the prediction of renal functional decline or the early detection of treatment responsiveness in Iraqi children with INS. This would necessitate the inclusion of a large number of patients from multiple centers in a cohort-designed work. The validation investigation should also study the uNGAL levels and other parameters of renal impairment and treatment response before starting NS therapy and prospectively follow the patients for prolonged periods.

The purpose of urinary biomarker availability is not to replace the histological diagnosis with a biopsy. However, a urinary biomarker in combination with other clinical investigations can provide a source of valuable information to develop more impactful and personalized therapy approaches for children with NS.

Conclusion

The present study revealed that uNGALis capable of discriminating SRNS from SSNS in Iraqi children with significant reliability.

Author declarations

We hereby confirm that all the Figures and Tables in the manuscript are ours. Besides, the Figures and images, which are not ours, have been given permission for re-publication attached with the manuscript.-Authors sign on ethical consideration's approval-Ethical Clearance: The project was approved by the local ethical committee in College of Pharmacy / University of Baghdad according to the code number (RECAUBCP17102021A on 17/10/2021).

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Author contributions

Study conception & design: (Ali M Abd Alridha & Dheyaa J Kadhim). Literature search: (Ali M Abd Alridha & Dheyaa J Kadhim). Data acquisition: (Ali M Abd Alridha & Dheyaa J Kadhim). Data analysis & interpretation: Ali M Abd Alridha). Manuscript preparation: (Ali M Abd Alridha **&** Dheyaa J Kadhim). Manuscript editing & review: (Ali M Abd Alridha, Ayad HA Alkhazrajy **&** Dheyaa J Kadhim).

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دراسة مقطعية للمستويات البولية للايبوكالين المرتبط مع انزيم الجيلاتينيز لخلايا الدم النيوتروفيل واقترانها مع الإستجابة للأدوية الستيرويديةلدى عينة من الأطفال العراقيين المصابين بمتلازمةالتناذر الكلوي

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الخلاصة

خلفية البحث:متلازمة التناذر الكلوي المقاومة للأدوية الستيرويدية ترتبط بمضاعفات صحية خطيرة وعبء مالي كبير. وقدأبلغت الدراسات عن زيادة في المستويات البولية للايبوكالين المرتبط بانزيم الجيلاتينيز لخلايا الدم النيوتروفيلفي الأطفال المصابين بمتلازمة التناذر الكلوي مجهولة السبب.

الأهداف: تهدف هذه الدراسة الى تقييم إمكانيةاللايبوكالين على تمييز المرضى المصابين بمتلازمة التناذر الكلوي غير محددة السبب والمقاومة للأدوية الستيرويديةعن المتلازمة المستجيبة للأدوية الستيرويديةفي الأطفال العراقيين.

المنهجية والمرضى:تم في هذه الدراسة المقطعية جمع مجموعة من الأطفال (32) الذين يعانون المتلازمة المستجيبة للأدوية الستيرويدية ومجموعة أخرى من الأطفال (31) المصابين بالمتلازمة المقاومة للأدوية الستيرويدية من العيادة الإستشارية لأمراض كلى اللأطفال في مستشفى بابل للنسائية والأطفال لمدة ثلاثة أشهر. في هذه الدراسة، جمعت بيانات المرضى السريرية والتحاليل البولية وم قياس تركيزاللايبوكالين عبر الفحص المناعي الإنزيمي (ELISA) والمتوفر تجارياً.

النتائج:لوحظ بأن متوسطالمستويات البولية للايبوكالين أعلى بكثير ($p<0.001$) في مجموعة الأطفال الذين يعانون من المتلازمة المقاومة للادوية الستيرويدية[الوسيط (مدى الربعيات البينية) = 131.512(30.28) نانوغرام / مل] مقارنة بمجموعة الأطفال الذين يعانون من المتلازمة المستجيبة للادوية الستيرويدية [الوسيط (مدى الربعيات البينية) = 88.45 (41.6) نانوغرام / مل]. كما وقد كان هناك إرتباط سلبيبين المستويات البولية للايبوكالين ومعدل الترشيح الكبيبي المقدر (eGFR) [معامل رو سبيرمان=- 0.599، $p<0.001$]. وعلى الرغم من ذلك، فقد كانت هناك تراكيز عالية نسبيًا من اللايبوكالين لدى مرضى متلازمة التناذر الكلوي المقاومة للأدوية الستيرويدية والذين قدرت معدلات الترشيح الكبيبي لديهم بأكثر من 60 مل / دقيقة / 1.73 $م^2$.و بينت هذه الدراسة أيضًا أن القوة التمييزية للمستويات البولية للايبوكالين على تشخيص متلازمة التناذر الكلوي المقاومة للأدوية الستيرويديةعالية وبشكل ملحوظ [المساحة تحت منحني التنبؤ (AUC) =0.899،$p<0.0001$]. وقد كانت قيمة القطع المثالية والبالغة 111.091 نانوغرام / مل قادرة على الكشف التشخيصي للأطفال الذين يعانون من المتلازمة المقاومة للأدوية الستيرويدية وتفريقهم عن اولئك الذين يعانون منالمتلازمة المستجيبة للأدوية الستيرويدية بمستوى حساسية قدره 87.1 ٪ وبمستوى نوعية قدره 87.5٪.

الإستنتاجات: استنتجت هذه الدراسة أن اللايبوكالين له قدرة عالية على التشخيص التفريقي، وبدون اي وخز أو حقن، بين اللأطفال الذين يعانون منمتلازمة التناذرالكلوي المقاومة للأدوية الستيرويديةوتمييزهم عن اولئك الذين يعانون من المتلازمة المستجيبة للأدوية الستيرويدية.

الكلمات المفتاحية: مؤشر، لايبوكالين مرتبط بإنزيم الجيلاتينيز لخلايا الدم النيوتروفيل، التناذر الكلوي المقاوم للأدوية الستيرويدية، التناذر الكلوي المستجيب للأدوية الستيرويدية.