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Correlation between Urinary IL-6 and Renal Scan Isotope in Detecting Renal Scarring in Children with Obstructive Nephropathy

AHMED ABDALLAH MOHAMED, M.D.; BASMA S. KARAM, M.Sc.; MOHAMED N. EL-SHARAWI, M.D. and NORA NABIL A. AHMED, M.D.

The Department of Pediatrics, Faculty of Medicine, Ain Shams University

Abstract

Background: Obstructive Nephropathy is any affection of the urinary tract characterized by impairment of urine flow through the tract and which, if left untreated, will cause progressive renal scarring. Interleukin-6 (IL-6) has been extensively studied in children with obstructive nephropathy, focusing on its association with renal scarring. Studies have shown elevated IL-6 levels in children with renal scarring, suggesting its potential as a biomarker for renal inflammation and scarring.

Aim of Study: To evaluate the correlation between urinary IL-6 and renal scan in detecting renal scarring in children with obstructive nephropathy.

Patients and Methods: This study is an observational casecontrol study. This study was conducted at Pediatric Nephrology Department, Children's Hospital, Ain Shams University. The study period was 6 months. The study population was 15 admitted cases of proven obstructive nephropathy in an acute attack of pyelonephritis and 15 healthy matched controls.For all enrolled cases, full history was taken including age at diagnosis, presenting complaint on admission and past history of previous operations. Full clinical examination was conducted, laboratory investigations were done including kidney function tests, urine analysis, IL-6 level in urine and radiological investigations including pelvi abdominal ultrasound and DMSA scan.

Results: Mean age of the study group was 6 years and 73% were males without any significant statistical difference between the two groups in age or sex. Majority of the cases were diagnosed as posterior urethral valve with bilateral vesicoureteric reflux and bilateral hydronephrosis, other diagnoses included primary vesicoureteric reflux, neurogenic bladder and ureteric stones.Our study showed that Our study investigated the correlation between urinary IL-6 levels, DMSA renal scans, and chronic kidney disease (CKD) grades in children with obstructive nephropathy. While we found that there was statisticall significant increase in cases than control groups regarding IL-6 level and that the level significally decreased after resolution of the attack of pyelonephritis (p<0.001), we didn't observe a significant correlation between IL-6 levels and DMSA renal scan findings. Additionally, there was no significant correlation between IL-6 levels and different grades of CKD.

Conclusion: This study found significantly elevated urinary IL-6 levels in cases compared to controls during acute pyelonephritis and even after resolution but we didn't observe a significant correlation between IL-6 levels and DMSA renal scan findings. Our findings suggest that while urinary IL-6 may serve as a marker of renal inflammation, it may not directly correlate with the extent of renal scarring or the severity of CKD in pediatric patients with obstructive nephropathy.

Key Words: *Urinary IL-6 – Renal Scan Isotope – Renal Scarring – Obstructive Nephropathy.*

Introduction

OBSTRUCTIVE nephropathy refers to the mechanical or functional changes in the urinary tract that interfere with normal urinary flow; Once obstruction is set, it leads to progressive renal damage that is mainly characterized with tubulointerstitial fibrosis **[1].**

Causes of obstructive nephropathy in children could be congenital or acquired. Congenital causes could be pelvi-ureteric junction obstruction, posterior urethral valves (PUV), urethral atresia, phimosis, meatal stenosis and neurogenic bladder. The acquired causes could be calculi, post-traumatic and post-inflammatory strictures and meatal stenosis **[2].**

In UTIs differentiation between acute pyelonephritis (APN) and lower urinary tract infection (LUTI) is recommended because of their therapeutic and prognostic consequences **[3].**

Defense against mucosal infections relies on chemokines that engage inflammatory cells to the

Correspondence to: Dr. Basma S. Karam,
E-Mail: Basmasamehkaram@gmail.com

mucosa. Pro-inflammatory cytokines, particularly interleukin-6 (IL-6), determined in urine (uIL-6) or serum (sIL-6), have been shown to be useful as biological indicators of renal involvement in UTI **[4].**

IL-6 is secreted by uroepithelial cells in response to bacterial invasion, particularly P-fimbriated Escherichia coli. In healthy children, IL-6 is found in only small quantities **[5]**, but it has been found to be elevated in the renal tissue of patients with kidney diseases, including diabetic nephropathy, glomerulonephritis and obstructive nephropathy **[6].**

Analysis of such urinary tract infections includes urine culture & sensitivity, ultrasonography (US), micturating cystourethrogram (MCUG), cystoscopy and dimercaptosuccinic acid (DMSA) renal scan for a complete evaluation. Renal scarring following an attack of UTI can be diagnosed by DMSA scan, which is the gold standard **[7].**

DMSA, as a non-invasive modality to test the renal parenchymal involvement, can be included to detect renal scars during follow-up of infants after the first attack of UTI **[8].**

Aim of the work:

To evaluate the correlation between urinary IL-6 and renal scan in detecting renal scarring in children with obstructive nephropathy.

Patients and Methods

Subjects: This case control study was carried out in Ain Shams University Pediatric Hospital, in the period between January 2023 and January 2024. Included thirty (30) pediatric subjects divided into two groups:

- Group (1): Cases with obstructive nephropathy: 15 children less than 14 years of age diagnosed with obstructive nephropathy and admitted in Pediatric Nephrology Unit Ward, Ain Shams University.
- Group (2): Control group: 15 healthy children and adolescents, attending pediatric ER or clinic with negative past and family history of renal disease (matching with patient group in age and sex).

Inclusion criteria: Infants, children and adolescents less than 14 years of age, with culture positive febrile urinary tract infection with proven obstructive nephropathies following-up in our Pediatric Nephrology Clinic, Ain Shams University.

Exclusion criteria: Concomitant febrile disease other than UTI affecting IL-6 levels and anomalies that hinder urine analysis as bladder extrophy, diabetic nephropathy and glomerulonephritis.

Prior to initiation, the study was approved by the ethical committee of the Faculty of Medicine, Ain Shams University (FMASU MD) assurance no FWA 000017585 and all participants first degree relatives provided informed verbal consent.

Laboratory work was conducted in the Clinical Pathology Department, Ain Shams University Hospital.

All patients were subjected to the following: Full history taking including: Personal history: Full name, age and sex. History of present illness: Age at onset of symptoms, course and duration, age at diagnosis, presenting symptoms during this hospital admission with stress on manifestations of pyelonephritis: Fever, lethargy, loin pain, dysuria, urgency, frequency and hematuria and duration of hospital admission and antibiotics taken during this admission at which IL-6 was collected. Past History: previous operations as vesicostomy, pyeloplasty and ureteric implantation, previous hospital admissions with stress on toxic symptoms of pyelonephritis and history of elevated kidney functions and previous NICU or PICU admissions. Family History: Consanguinity, similar medical condition of renal affection and chronic diseases. Antenatal and Postnatal History: oligohydraminos or any renal anomalies diagnosed by antenatal ultrasound.

Physical examination: Anthropometric measurements: Weight in kg, height in cm and plotting them on the age and sex standard percentiles according to CDC child growth charts. (Centers for Disease Control and Prevention, National Center for Health Statistics, 2022) and body mass index (BMI): Was calculated as weight in (kg) / height in (m^2), the obtained number was plotted on appropriate CDC gender-specific BMI-for-age growth chart to determine BMI percentile. Complexion: Pallor, Jaundice. Lymph nodes examination. Abdominal examination for vesicostomy, mitrofanoff and renal angle tenderness.

Methods: A-Laboratory investigations: Were done for the patients during their hospital admission. 1. Complete blood count (CBC) including total leucocytic count (10^3/UL) with manual differential, hemoglobin (g/dl), Platelets (10^3/UL). 2. Kidney Function tests including BUN (mg/dl), serum creatinine (mg/dl).

Glomerular filtration rate (GFR) was calculated using Schwartz equation: CrCl (ml/min/1.73m^2)= (Height (cm) x k)/ Serum Creatinine.

*k = 0.55 for children 1 to 13 years old

CKD grading was done according to GFR using National Kidney Foundation guidelines.

Table (1): Stages of chronic kidney disease and clinical action PLANS33.

Stage	Description	GFR
G1	Kidney damage with normal or 1 GFR	≥90
G2	Kidney damage with mild: GFR	60-89
G3	Moderate: GFR	30-59
G4	Sever: GFR	15-29
G5	Kidney failure	<15

3. Serum albumin level (g/dl). 4. C- reactive protein (mg/l). 5.Erythrocyte sedimentation rate (mm/hr). 6. Urine analysis: mid-stream urine sample or urine collected by urinary catheter including specific gravity, pus cells, red blood cells and nitrites.7. Urine culture and sensitivity with colony count.

Urinary IL-6 (ng/l): First urine sample was collected from patients on admission in sterile urine cups, either mid-stream urine sample or collected by urinary catheter in already catheterized patients. Second urine sample was collected from patients one month after their discharge from hospital and resolution of the attack of pyelonephritis.

Samples were stored at –80 degree Celsius and then IL-6 (ng/l) was measured by enzyme linked immunoassay (ELISA) kits.

Pelviabdominal ultrasound: Was performed for all patients early on admission in Pediatric Radiology Unit, Ain Shams University.

DMSA Scan: Was performed for all patients one month after resolution of the attack of pyelonephritis as after their discharge from hospital. Renal scars were identified and graded as per the standard classification.

These grades are classified as follow: Grade (0): No cortical scars. Grade (1): No more than two scars. Grade (2): More than two scars with some normal parenchyma between them. Grade (3): Generalized damage to the whole kidney. Grade (4): End stage (kidney with little or no uptake of DMSA, I.E., <10% of the overall function) **[7].**

Data management and analysis: The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 27). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics: (1) Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. (2) Frequency and percentage of non-numerical data.

Analytical statistics: (1) Mann Whitney Test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. (2) Fisher's exact test was used to examine the relationship between two qualitative variables. (3) Correlation analysis (using Spearman's rho method) to assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "*r*" defines the strength (magnitude) and direction (positive or negative) of the linear relationship between two variables: *r*=0-0.19 is regarded as very weak correlation. *r*=0.2-0.39 as weak correlation. *r*=0.40-0.59 as moderate correlation. *r*=0.6-0.79 as strong correlation. *r*=0.8-1 as very strong correlation.

Wilcoxon signed rank test was used to assess the statistical significance of the difference of an ordinal variable (score) measured twice for the same study group.

The Kruskal-Wallis test was used to assess the statistical significance of the difference between more than two study group ordinal variables.

p-value: Level of significance: $p>0.05$: Non significant (NS). $p<0.05$: Significant (S).

Results

This study was conducted on 30 subjects divided equally into two groups controls and cases of obstructive nephropathy, Table (2) shows demographic data, the mean age of the study group was 6.17±3.51 year old, while most subjects were males by 73.3% without any significant difference between two groups in age nor sex.

Table (2): Socio demographic data between two study groups.

	Group		Test of significance		
	Controls (N=15)	Cases (N=15)	Value	*p*-value	Sig.
ge (Years):					
Mean ± SD	6.2±3.51	6.17±3.51	z = –0.042	0.967	NS
Median (IQR)	6 (3 - 8)	6 (3 - 8)			
Sex N (%):					
Male	11 (73.33%)	11 (73.33%)	FE	1.00	NS
Female	4 (26.67%)	4 (26.67%)			

*Mann-Whitney test of significance (z).
*Fisher's Exact test of significance.

Table (3) illustrates description for sociodemographic data within cases group only, most of patients hadn't history of consanguinity by 80%, regarding anthropometric measures 46.7% of patients were underweight and normal height and were underweight by BMI. 73.3% of theses patient didn't need NICU admission.

Table (4), demonstrates illness data within cases group only, regarding diagnosis about third of patients had (PUV + Bilateral hydronephrosis + Bilateral VUR), other third had (Primary Bilateral VUR) and the last third other diagnoses. More than half of patients had acute onset and progressive course.

Third of patients diagnosed with obstructive nephropathy at their first year of life and 40% after first year.

Table (5) shows presenting symptoms for cases group, the most presenting symptom was fever by 80%, followed by vomiting by 46.7% then loin pain by 40%, while the least frequent one was convulsion by 13.3% of patients.

Table (6) illustrates grades of CKD according eGFR (ml/min/1.73 m^2), the mean GFR was 86.6 ± 59.58 and ranged from 28.5 -222. Most of patients had grade 3 by 46.7%, 40% had grade 1, while the least grade was grade 2 by 13.3%.

Table (7) present risk factors within cases group onlyfor developing renal scars, previous operations was the most frequent risk factor by 80%, recurrent attacks were 73.3% and elevated KFT were found in 60% of cases.

Table (3): Sociodemographic data within the cases group only.

	N	%
Consanguinity:		
No	12	80.0
Yes	3	20.0
Weight:		
Underweight	7	46.7
Normal weight	8	53.3
Height:		
Stunted	8	53.3
Normal height	7	46.7
BMI:		
Underweight	7	46.7
Normal BMI	6	40.0
Overweight	2	13.3
NICU admission:		
No	11	73.3
Yes	4	26.7

Table (4): Illness data within the cases group only.

	N	%
Diagnosis:		
PUV + Bilateral hydronephrosis + Bilateral VUR	5	33.3
PUV + Unilateral hydronephrosis + Unilateral VUR	1	6.7
Primary Bilateral VUR	5	33.3
Neurogenic bladder	3	20.0
Unilateral Ureteric stones	1	6.7
Onset of symptoms:		
Acute	8	53.3
Gradual	7	46.7
Course:		
Progressive	9	60.0
Intermittent	6	40.0
Duration:		
Since birth	4	26.7
First year of life	5	33.3
After 1st year	6	40.0

Table (5): Symptoms within the cases group only.

	N	%
Fever	12	80.0
Vomiting	7	46.7
Loin pain	6	40.0
Lethargy	5	33.3
Hematuria	5	33.3
Convulsion	2	13.3

Table (6): CKD grading (according eGFR) & GFR within the cases group only.

	Mean ± SD N (%)	Median (IQR)	Range
GFR (ml/min/1.73 m^2)	86.6±59.58	63 (35 - 114)	(28.5 - 222)
CKD:			
1	6 (40.0%)		
2	2 (13.3%)		
3	7 (46.7%)		

Table (7): Risk factors for developing renal scarswithin the cases group only.

	N	%
Operations	12	80.0
Recurrent attacks	11	73.3
Elevated KFT	9	60.0

Table (8) demonstrates lab investigations within cases group only, the TLC (10^3/ul) mean group was 10.18±3.89, the Neut (10^3/ul) mean was 9.74±15.95, and the Lym (10^3/ul) mean was 6.76±13.52. The table also shows that the most prevalent organism detected in the cases group is Klebsiella, accounting for 46.67%, while Candida nonalbicans was found only in one case, comprising 6.67%.

Table (8): Lab investigations within the cases group only.

	Mean ± SDN (%)	Median (IQR)	Range
TLC (10^3/ul)	10.18±3.89	11 (6.2-12.8)	(5.18-18.9)
Neut (10^3/ul)	9.74±15.95	4.8 (3.5-9.8)	(1.05-66)
Lym (10^3/ul)	6.76±13.52	2.7 (1.9-3.8)	(1.3-55)
Hb (g/dl)	10.67±1.75	11 (9.3-11.6)	(7.8-13.3)
PLT (10^3/ul)	360.93±157.85	392 (247-450)	(48-662)
Creat (mg/dl)	0.89±0.53	0.7 (0.5-1.3)	(0.26-1.9)
BUN (mg/dl)	20.67±9.89	22 (12-28)	(4-41)
Albumin (g/dl)	3.80±0.38	4 (3.6-4)	(3-4.3)
CRP (mg/l)	61.89±52.47	41 (20-91)	(3.2-168)
ESR (mm/hr)	36.07±27.49	30 (10-50)	(5-90)
Pus cells:			
Abnormal	15 (100%)		
RBCs:			
Normal	7 (46.67%)		
Abnormal	8 (53.33%)		
SP gravity:			
Normal	15 (100%)		
Nitrites:			
Absent	13 (86.67%)		
1	1 (6.67%)		
2	1 (6.67%)		
Organism:			
Klebsiella	7 (46.67%)		
E. coli	3 (20%)		
Pseudomonas	2 (13.33%)		
Staphaureus	2 (13.33%)		
Candida nonalbicans	1 (6.67%)		

TLC : Total leucocytic count.
Neut : Neutrophils.
Lym : Lymphocytes.
Hb : Hemoglobin.
Plt : Platelets.
Creat: Serum creatinine.
BUN : Blood urea nitrogen.
CRP : c- reactive protein.
ESR : Erythrocyte sedimentation rate.
RBCs: Red blood cells.
SP : Specific gravity.

Table (9) shows U/S findings within cases group only, most patients had finding bilaterally by 73.3%, and the most prevalent finding was Hydroureterunephrosis found in 46.7%, followed by Hydronephrosis in 33.3%, while Pyonephrosis found in only 20% of cases.

Table (10) presents prevalence of positive cases for reflux by MCUG and it was positive in 46.7% of cases who underwent a MCUG.

Table (9): U/S findings within the cases group only.

	N	%
U/S:		
Bilateral	11	73.3
Left	4	26.7
U/S findings:		
Hydroureterunephrosis	7	46.7
Hydronephrosis	5	33.3
Pyonephrosis	3	20.0

Table (10): MCUG within the cases group only.

	N	%
MCUG:		
Positive	7	46.7
Not assessed	8	53.3

Table (11): IL-6 results in urin (ng/L).

IL-6 result in urine	Controls	Cases	*t*-test		
			t	*p*-value	Sig.
On acute attack	18.51± 8.88	267.92± 96.43	-9.98	<0.001	S
1 month after resolved	18.51± 8.88	226.03± 91.63	-8.73	<0.001	S

This table shows the results of a t test comparing the levels of IL-6 in the urine samples of controls and cases. The cases are patients who had an acute attack. The table shows that the cases had significantly higher levels of IL-6 than the controls, both during the acute attack and one month after the attack was resolved.

Table (12): Renal scan assessment within the cases group only.

	N	%
RT renal scan:		
Grade 0	8	53.3
Grade I	5	33.3
Grade II	1	6.7
Grade III	1	6.7
Lt renal scan:		
Grade 0	7	46.7
Grade I	3	20.0
Grade II	2	13.3
Grade III	3	20.0

Table (12) reports the results of renal scan assessments on both sides within the cases group only, for the RT renal scan, the most common grade was Grade 0, which was observed in 8 cases (53.3%), followed by Grade I with 5 cases (33.3%). Only one case (6.7%) exhibited Grade II and III on the RT renal scan. On the Lt renal scan, Grade 0 was also the most common, occurring in 7 cases (46.7%). Grade I is the second most common, with 3 cases (20%) followed by Grade III and Grade II, each present in 3 cases - 20% for both. The result of this table indicates that the majority of cases in this study had normal or mildly abnormal RT and Lt renal scan results.

Table (13) reports correlation between GFR (ml/min/1.73m^2) and IL-6 results in urine (ng/L) on acute attack and one month after resolved, there were no statistically significant correlation between them.

Table (14) shows correlation between renal scan and IL-6 results in urine (ng/L) on acute attack and one month after resolved, there were no statistically significant correlation between them.

Table (15) shows correlation between GFR (ml/min/1.73m^2) and renal scan, there was moderate negative statistically significant correlation between with right renal scan, while there was no statistically significant correlation with left renal scan.

Table (16) illustrates the relation between IL-6 results in urine (ng/L) on acute attack and one month after resolved and different grades of CKD, there were no statistically significant difference in both acute attack nor after one month later.

Table (17) reports the relation between both sides of renal scan and different grades of CKD, there was statistically significant difference with right renal scan as grade 3 CKD had more cases with renal scan grade 1 and less cases with grade 0 renal scan, while there was no statistically significant difference with left renal scan.

Table (13): Correlation between IL-6 results in urine (ng/L) and GFR (ml/min/1.73m^2).

	IL-6 result in urine (on acute attack)	IL-6 result in urine (1 month after resolved)
GFR (ml/min):		
Spearman's rho	0.054	0.300
p-value	0.850	0.277
Sig.	NS	NS

Table (14): Correlation between IL-6 results in urine (ng/L) and renal scan.

	RT renal scan	Lt renal scan
IL-6 result in urine (on acute attack):		
Spearman's rho	-0.265	0.000
p-value	0.339	1.000
Sig.	NS	NS
IL-6 result in urine (1 month after resolved):		
Spearman's rho	-0.479	0.133
p-value	0.071	0.637
Sig.	NS	NS

Table (15): Correlation between GFR (ml/min/1.73m^2) and renal scan.

	RT renal scan	Lt renal scan
GFR (ml/min/1.73m^2):		
Spearman's rho	-0.516	–0.351
p-value	0.049	0.199
Sig.	S	NS

Table (16): Relation between IL-6 (ng/L) on acute attack and 1 month after resolved & different grades of CKD within cases group.

IL-6 result in urine (ng/L)	CKD Grade			Kruskal Wallis test		
	1 (N= 6) Median (IQR)	2 (N= 2) Median (IQR)	3 (N=7) Median (IQR)	H	*p*-value	Sig.
On acute attack	274.1 (219 - 312.7)	231.95 (203.8 - 260.1)	198 (156.6 - 387.8)	1.408	0.495	S
1 Month after resolved	250.2 (226.7 - 261)	245.95 (236 - 255.9)	185 (123 - 203.8)	4.854	0.088	NS

Table (17): Relation between renal scan & different grades of CKD within cases group.

	CKD			Fisher's exact test	
	1 (N= 6) N (%)	2 (N= 2) N (%)	3 (N= 7) N (%)	*p*-value	Sig.
RT renal scan:					
Grade 0	5 (83.33%)***a***	2 (100%)***a***	1 (14.29%)***b***	0.012	S
Grade I	0 (0%)***a***	0 (0%)***a,b***	5 (71.43%)***b***		
Grade II	0 (0%)***a***	0 (0%)***a***	1 (14.29%)***a***		
Grade III	1 (16.67%)***a***	0 (0%)***a***	0 (0%)***a***		
Lt renal scan:					
Grade 0	1 (16.67%)	2 (100%)	4 (57.14%)	0.313	NS
Grade I	1 (16.67%)	0 (0%)	2 (28.57%)		
Grade II	1 (16.67%)	0 (0%)	1 (14.29%)		
Grade III	3 (50%)	0 (0%)	0 (0%)		

* Each subscript letter denotes a subset of Group categories whose column proportions do not differ significantly from each other at the 0.05 level.

Discussion

Interleukin-6 is a pro-inflammatory cytokine that plays a crucial role in immune responses and inflammation. It is produced by various cell types, including, immune cells, endothelial cells and renal tubular cells *[9]*.

The role of interleukin-6 in renal scarring has been the subject of numerous clinical studies in children with obstructive nephropathy *[10]*.

Measurement of IL-6 in urine can serve as a non-invasive method to assess the degree of renal inflammation and scarring *[11]*.

DMSA renal scan is frequently employed to evaluate the extent and severity of renal scarring and helps in identifying areas of focal or diffuse scaring (Hung et al., 2016). Despite its clinical utility, it has certain limitations and potential pitfalls that need to be considered *[12]*. On top of this limitations is the potential risks associated with radiation exposure, especially in pediatric patients *[13]*.

So in the current study, we sought to correlate between urinary IL-6 and DMSA renal scan in detecting renal scaring in children with obstructive nephropathy.

Our study was a case control study carried out in Ain Shams University, Pediatric Hospital, Nephrology Department.

We have recruited two groups; Group 1: 15 infants, children or adolescents less than 14 years of age with culture positive febrile UTI with proven obstructive nephropathy, admitted in in Pediatric Nephrology Unit Ward. Group 2: 15 healthy children matching with patient group in age and sex.

Regarding the demographic data, the median age of the study group was 6 years old, and 73% of the subjects were males, without any significant statistical difference between the two groups in either age or sex. As for anthropometric measures of the cases group, 46.7% were underweight, and 53.3% were stunted.

About diagnoses of our case group, one third of the patients had posterior urethral valve with bilateral hydronephrosis and bilateral VUR, one third had primary bilateral VUR, one third had other diagnoses as neurogenic bladder and renal stones.

This was in contrast to another descriptive observational study done in pediatrics by Mohammed and Elbehidy *[14]* which showed that neurogenic bladder dysfunction is the most common cause of obstructive nephropathy, followed by posterior urethral valves.

In our study, the most common presenting symptom in cases group was fever (80%), followed by vomiting, loin pain which agreed with meta-analysis by Leung et al. *[15]* which concluded that unexplained fever is the most common symptom of UTI during the first two years of life. After the second year of life, symptoms and signs of pyelonephritis include fever, chills, rigor, flank pain, and costovertebral angle tenderness.

Our study demonstrated that mean total leucocyte count was 10.8 and that CRP was elevated in cases during the attack who also had high levels of urine IL-6 as will be mentioned later. This agreed with Sheu et al. *[16]* who said that serum and urine IL-6 in children with acute pyelonephritis were positively correlated with fever, CRP and leucocyturia.

This could be explained that during infection or tissue damage, IL-6 is produced as part of the early immune response. It acts to activate immune cells, such as T cells and macrophages and production of acute phase proteins in liver including C-reactive protein *[17]*.

The most common organism detected by urine culture and sensitivity that was done to our study group during the attack of pyelonephritis was Klebsiella accounting for 46.6%.

On the contrary, Cross-sectional retrospective study on 104 Iranian children with pyelonephritis (37% of the patients had obstructive causes by ultrasound) showed that E. coli was the most frequent pathogen in urine samples so that this bacterium was present in samples of 96 patients (92.31%) *[18]*.

An Explanation to this is, in Egypt antibiotic resistance is increasing due to misuse of antibiotics and this was confirmed by Tarek et al. *[19]* cross sectional study done in Egypt using 15,252 urine samples; Klebsiella species were the most MDR and extended-spectrum β-lactamase (ESBL)-producing organisms.

In our study, urine IL-6 was measured for the cases group during the attack of pyelonephritis and 1 month after resolution of the attack. It was also measured for the control group.

Comparing the two studied groups: it showed that the cases had significantly higher levels of urinary IL-6 than the controls, both during the acute attack of pyelonephritis ($p<0.001$) and one month after the attack resolved ($p<0.001$)

These results were in agreement with Yu et al. *[20]* cohort study that enrolled 17 patients with Uretero Pelvic Junction Obstruction (UPJO) and 17 healthy matched subjects, showed significantly elevated IL-6 in the urine from individuals with UPJO compared with controls ($p= 0.00073$).

Also a systemic review and meta-analysis done by Hosseini et al. *[21]* showed that the diagnostic utility of ILs 6 and 8 urinary levels is most desirable in the detection of febrile UTIs from other febrile conditions in children and adolescents, in comparison with the diagnostic utility of other ILs' urinary and serum levels in the detection of febrile UTI.

In contrast to the study of Haraoka et al. *[22]* which measured urine IL-6 levels in 32 patients with VUR, and levels were below the lower detection limit in all samples.

Explanation: IL-6 is a pro-inflammatory cytokine involved in the immune response during UTIs and in the inflammatory processes that occur in the renal parenchyma, with possible involvement in the pathophysiology of reflux nephropathy. Most of the studies reported the presence of increased concentrations of urinary IL-6 in patients with VUR or renal scarring *[23-25]*.

In the kidneys, IL-6 is secreted by tubular, mesangial, and endothelial cells, and is involved in local inflammatory processes. Immunohistochemical assessments performed in patients with RN have shown that areas of increased IL-6 synthesis are located near areas of fibrosis. These aspects support the possible involvement of IL-6 in the pathophysiology of VUR and RN *[26-27]*.

Another pathophysiological aspect that supports the increased expression of urinary cytokines in patients with VUR and RN is linked to Toll-like receptors (TLRs). TLRs are involved in the innate immune response during UTIs, resulting in proinflammatory cytokine secretion, such as IL-6. TLR4 is upregulated in the kidneys after parenchymal injury *[28]*.

Obstruction of the urinary tract may decrease renal blood flow and the glomerular filtration rate *[29]*.

In our study, eGFR of the cases was calculated using Schwartz pediatric bedside formula (0.55 x height in cm/serum creatinine) and then CKD graded according to Stages of Chronic Kidney disease by National Kidney Foundation. The mean eGFR for the cases was 86.6 ml/min/1.73m^2 and most of the patients had Grade 3 CKD by 46.7%, 40% had Grade 1 CKD, and 13.3% had Grade 2 CKD according to National kidney foundation CKD grading.

In another study, sixty-three previously treated patients with posterior urethral valve were evaluated for renal function. They found that twenty of the study patients (32%) had decreased GFR Heikkilä et al. *[30]*.

In contrast to our study, the retrospective cross-sectional study done by Rodríguez et al. *[31]*, including 383 patients with congenital obstructive nephropathies, showed that 95 (24.8%) patients had chronic renal disease, with 86% classified as grade 2, after analyzing their GFR.

Our study tried to correlate urinary IL-6 levels and different grades of CKD guided by patients' eGFR, but there was no significant statistical correlation between them.

There were no enough studies done in pediatrics patients trying to correlate this relation.

Some studies conducted in adults suggested a statistical correlation between IL-6 levels and the evolution of chronic kidney disease. For instance, the study done by Shankar et al. *[32]*, which involved a population-based cohort of 4926 participants, showed that circulating levels of IL-6 and TNF-α receptor 2 were associated with incident CKD.

Furthermore, another study done by Amdur et al. *[33]* demonstrated that elevated plasma levels of fibrinogen, IL-6, and TNF-α, along with decreased serum albumin, were significantly associated with

a composite outcome of End Stage Renal Disease (ESRD) or a reduction of 50% in the eGFR from baseline.

In our study, the entire cases group had done a renal ultrasound showing that: 73.3% had bilateral findings, and the most prevalent finding was hydroureteronephrosis which was found in 46.7%, followed by hydronephrosis in 33.3%, while pyonephrosis found in only 20% of the cases.

Ultrasound is considered the gold standard in the diagnosis of obstructive uropathy: it allows distinguishing three degrees of urinary tract dilation, depending on the extent of the dilation itself and the thickness of the parenchyma **[34].**

DMSA scans have been recommended for the evaluation of dilated upper urinary tract and renal scarring following refluxing and non-refluxing pyelonephritis in children **[35].**

In a prospective study to evaluate renal scars done by Shanon et al. **[36]** DMSA scan served as the gold standard in detection in renal scars, it was sensitive by (94%) and specific by (100%) in identifying renal scars in children.

In our study, majority of the cases had normal or mildly abnormal Right and Left renal scan results. That was graded as the Standard Classification **[7].**

- Grade 0: No cortical scar
- Grade 1: No more than two scars.
- Grade 2: More than two scars with some normal parenchyma between them.
- Grade 3: Generalised damage to the whole kidney.
- Grade 4: End stage (kidney with little or no uptake of DMSA).

Right renal scan, most common grade was grade 0 (53.3%), followed by grade 1 (33.3%), (6.7%) for grades 2 and 3.

Left renal scan, most common was grade 0 (46.7%), followed by grade 1 and grade 3 (20%), while grade 2 (13.3%).

Our study tried to correlate between IL-6 level and DMSA scan in detection of renal scars but there was no statistical significant between them. However this was maybe due to the following reasons:

1- Small sample size as patients weren't compliant to do the DMSA scan due to its radiation hazards and fear of anesthesia complications.
2- Timing of DMSA scan is best to be done after acute infection has been treated and resolved, usually 4-6 weeks later to accurately evaluate the presence and extent of renal scarring **[37].**

With our study, this study Gupta et al. **[38]** investigated for differences in markers of trans IL-6 signaling between patients with a history of febrile UTI with and without renal scarring. There was no significant difference between the absolute values or ratio of IL-6 between those with and without scarring.

In contrast to our study, a study on 79 children by Sheu et al. **[39]** showed that both serum and urine IL-6 levels during the acute phase of pyelonephritis were significantly higher in children with renal scarring (assessed by DMSA Scan) than in those without (p=0.005 and p=0.002).

We also tried to correlate DMSA scan and different grades of CKD within cases group, there was statistical significant difference with right renal scan as Grade 3 CKD had more cases with renal scan Grade 1 and less cases with Grade 0 renal scan, while there was no statistical significance difference with left renal scan.

The explanation to this:

A number of studies have shown that the relative uptake of DMSA correlates well with the relative estimated renal plasma flow (ERPF) and GFR in patients with both normal and asymmetrically functioning kidneys, another few investigators have reported DMSA scanning may be misleading in patients with obstruction due to retention of DMSA in the renal pelvis. This conclusion is based on a discrepancy in the relative renal function determined using DMSA and 131 I-hippurate or DTPA **[40].**

Also DMSA scan while assessing the renal cortex, lacks detailed information about renal vasculature, collecting system and overall renal function **[41].**

DMSA scan requires proper patient preparation and cooperation to obtain accurate results. Patient movement, inadequate bladder filling or technical issues with the imaging equipment can lead to inconclusive or suboptimal images (Loewen & Greenbaum, 2022) **[42].**

Since a number of variables can affect the total renal accumulation of DMSA, DMSA should not be quantitated as an absolute index of renal function unless it is done by experienced investigators under carefully controlled conditions **[40].**

Conclusion:

We found significantly elevated urinary IL-6 levels in cases compared to controls during acute pyelonephritis and even after resolution but we didn't observe a significant correlation between IL-6 levels and DMSA renal scan findings. Additionally, there was no significant correlation between IL-6 levels and different grades of CKD. Our findings suggest that while urinary IL-6 may serve as a marker of renal inflammation, it may not directly correlate with the extent of renal scarring or the severity of CKD in pediatric patients with obstructive nephropathy.

References

1- ISHIDOYA S., KANETO H., FUKUZAKI A., TAKEDA A., OGATA Y., NAKAGAWA H., et al.: Pathophysiology and clinical implication of obstructive nephropathy. Nihon HinyokikaGakkaizasshi. The Japanese Journal of Urology, 94 (7): 645-655, 2003.

2- FERDOUS S., ROY R.R., AHMMED M.F. and SHAZZAD M.N.: Obstructive Nephropathy in Children-A Review. Bangladesh Medical Journal, 46 (3): 107-113, 2019.

3- FAHIMI D., KHEDMAT L., AFSHIN A., NOPARAST Z., JAFARIPOR M., BEIGI E.H., et al.: Clinical manifestations, laboratory markers and renal ultrasonographic examinations in 1-month to 12-year-old Iranian children with pyelonephritis: A six-year cross-sectional retrospective study. BMC Infectious Diseases, 21 (1): 1-9, 2021.

4- AZAB S., ZAKARIA M., RAAFAT M. and SEIEF H.: The combination of urinary IL-6 and renal biometry as useful diagnostic tools to differentiate acute pyelonephritis from lower urinary tract infection. International Braz J. Urol., 42 (3): 810-816, 2016.

5- CHING C.B., GUPTA S., LI B., CORTADO H., MAYNE N., JACKSON A.R., et al.: Interleukin-6/Stat3 signaling has an essential role in the host antimicrobial response to urinary tract infection. Kidney International, 93 (6): 1320-1329, 2018.

6- MAGNO A.L., HERAT L.Y., CARNAGARIN R., SCHLAICH M.P. and MATTHEWS V.B.: Current knowledge of IL-6 cytokine family members in acute and chronic kidney disease. Biomedicines, 7 (1): 19-25, 2019.

7- BANDARI B., SINDGIKAR SP., KUMAR S.S., VIJAYA M.S. and SHANKAR R.: Renal scarring following urinary tract infections in children. Sudanese journal of paediatrics, 19 (1): 25-30, 2019.

8- ABOUTALEB H., ABOUELGREED T.A., EL-HAGRASI H., BAKRYELDIB D., ABDELAAL M.A. and EL GOHARY M.A.: Correlation of Renal Scarring to Urinary Tract Infections and Vesicoureteral Reflux in Children. Arab Journal of Urology, 16 (1): 9-10, 2022.

9- VILLAR-FINCHEIRA P., SANHUEZA-OLIVARES F., NORAMBUENA-SOTO I., CANCINO-ARENAS N., HERNANDEZ-VARGAS F., TRONCOSO R. and CHIONG M.: Role of interleukin-6 in vascular health and disease. Frontiers in molecular biosciences, 8: 641734, 2021.

10- KOCAASLAN R., DILLI D. and ÇITLI R.: Diagnostic Value of the Systemic Immune-Inflammation Index in Newborns with Urinary Tract Infection. American Journal of Perinatology, 2022.

11- OPPEGAARD K.R., ARMSTRONG T.S., ANGUERA J.A., KOBER K.M., KELLY D.L., LAISTER R.C. and MAYO S.J.: Blood-based biomarkers of cancer-related cognitive impairment in non-central nervous system cancer: A scoping review. Critical Reviews in Oncology/Hematology, 180: 103822, 2022.

12- WAN S., YI Q., FAN, S. LV J., ZHANG X., GUO L. and CHEN Y.: Characteristics of lymphocyte subsets and cytokines in peripheral blood of 123 hospitalized patients with 2019 novel coronavirus pneumonia (NCP). MedRxiv., 2020.

13- FRIED J.G. and MORGAN M.A.: Renal imaging: Core curriculum 2019. American Journal of Kidney Diseases, 73 (4): 552-565, 2019.

14- MOHAMMED D.Y. and ELBEHIDY R.M.: Prevalence of Obstructive Uropathy in East Delta Children, 9 (2): 57-64, 2009.

15- LEUNG A.K., WONG A.H., LEUNG A.A. and HON K.L.: Urinary tract infection in children. Recent patents on inflammation & allergy drug discovery, 13 (1): 2-18, 2019.

16- SHEU J.N., CHEN M.C., LUE K.H., CHENG S.L., LEE I.C., CHEN S.M. and TSAY G.J.: Serum and urine levels of interleukin-6 and interleukin-8 in children with acute pyelonephritis. Cytokine, 36 (5-6): 276-282, 2006.

17- HIRANO T.: IL-6 in inflammation, autoimmunity and cancer. International immunology, 33 (3): 127-148, 2021.

18- FAHIMI D., KHEDMAT L., AFSHIN A., NOPARAST Z., JAFARIPOR M., BEIGI E.H. and MOJTAHEDI S.Y.: Clinical Manifestations, Laboratory Markers, and Renal UltrasonographicExaminationsin 1-month to12-year-old Iranian Children with Pyelonephritis: A Six-year Cross-sectional Retrospective study, 2020.

19- TAREK A., ABDALLA S., DOKMAK N.A., AHMED A.A., EL-MAHDY T.S., SAFWAT N.A. and EL-MAHDY IV, T.S.: Bacterial Diversity and Antibiotic Resistance Patterns of Community-Acquired Urinary Tract Infections in Mega Size Clinical Samples of Egyptian Patients: A Cross-Sectional Study. Cureus, 16 (1), 2024.

20- YU L., ZHOU L., LI Q., LI S., LUO X., ZHANG C. and-SUN H.: Elevated urinary lipocalin-2, interleukin-6 and monocyte chemoattractant protein-1 levels in children with congenital ureteropelvic junction obstruction. Journal of Pediatric Urology, 15 (1): 44-e1, 2019.

21- HOSSEINI M., AHMADZADEH H., TOLOUI A., AHMADZADEH K., NEISHABOORI A.M., ALAVI S.N.R. and ATAEI N.: The value of interleukin levels in the diagnosis of febrile urinary tract infections in children and adolescents; a systematic review and meta-analysis. Journal of Pediatric Urology, 18 (2): 211-223, 2022.

22- HARAOKA M., SENOH K., OGATA N., FURUKAWA M., MATSUMOTO T. and KUMAZAWA J.: Elevated interleukin-8 levels in the urine of children with renal scarring and/or vesicoureteral reflux. The Journal of Urology, 155 (2): 678-680, 1996.

23- KRZEMIEŃ G., ROSZKOWSKA-BLAIM M., KOSTRO I., SZMIGIELSKA A., KARPIŃSKA M., SIENIAWSKA M. and TOTH K.: Urinary levels of interleukin-6 and interleukin-8 in children with urinary tract infections to age 2. Medical Science Monitor, 10 (11): CR593-CR597, 2004.

24- GOKCE I., ALPAY H., BIYIKLI N., UNLUGUZEL G., DEDE F. and TOPUZOGLU A.: Urinary levels of interleukin-6 and interleukin-8 in patients with vesicoureteral reflux and renal parenchymal scar. Pediatric Nephrology, 25: 905-912, 2010.

25- NICKAVAR A., SAFAEIAN B., VALAVI E. and DAVOODI, H.: Utility of Urine Interleukines in Children with Vesicoureteral Reflux and Renal Parenchymal Damage. Urology Journal, 18 (02): 199-202, 2020.

26- SUNDÉN F., BUTLER D. and WULLT B.: Triggered urine interleukin-6 correlates to severity of symptoms in nonfebrile lower urinary tract infections. The Journal of Urology, 198 (1): 107-115, 2017.

27- JANTAUSCH B.A., O'DONNELL R. and WIEDERMANN B.L.: Urinary interleukin-6 and interleukin-8 in children with urinary tract infection. Pediatric Nephrology, 15: 236-240, 2000.

28- ANDERS H.J., BANAS B. and SCHLÖNDORFF D.: Signaling danger: Toll-like receptors and their potential roles in kidney disease. Journal of the American Society of Nephrology, 15 (4): 854-867, 2004.

29- KLAHR S.: Obstructive nephropathy. Internal Medicine, 39 (5): 355-361, 2000.

30- HEIKKILÄ J., JAHNUKAINEN T., HOLMBERG C. and TASKINEN S.: Association of renal glomerular and tubular function with renal outcome in patients with posterior urethral valves. Urology, 153: 285-290, 2021.

31- RODRÍGUEZ M.R., GAMERO M.A., HERNÁNDEZ A.P., TORRES S.R., CRUZ V.V. and ESTEBAN R.M.: Congenital malformations of the urinary tract: Progression to chronic renal disease. Cirugia Pediatrica (English Edition), 35 (4), 2022.

32- SHANKAR A., SUN L., KLEIN B.E., LEE K.E., MUNTNER P., JAVIER F.N. and KLEIN R.: Markers of inflammation predict the long-term risk of developing chronic kidney disease: A population-based cohort study. Kidney International, 80 (11): 1231-1238, 2011.

33- AMDUR R.L., FELDMAN H.I., GUPTA J., YANG W., KANETSKY P., SHLIPAK M. and CRIC Study Investigators: Inflammation and progression of CKD: The CRIC study. Clinical journal of the American Society of Nephrology, 11 (9): 1546-1556, 2016.

34- FIORINI F., DE PASCALIS A., D'AMELIO A., DI IORIO B., ABATERUSSO C. and GRANATA A.: Native kidney ultrasound in obstructive uropathy. Giornale Italiano di Nefrologia: Organo Ufficiale Della Societa Italiana di Nefrologia, 37 (1), 2020.

35- PADHI R., KABI S., PANDA B.N. and JAGATI S.: Prognostic significance of nonthyroidal illness syndrome in critically ill adult patients with sepsis. International journal of critical illness and injury science, 8 (3): 165-172, 2018.

36- SHANON A., FELDMAN W., MCDONALD P., MARTIN D.J., MATZINGER M.A., SHILLINGER J.F. and WOLFISH N.: Evaluation of renal scars by technetium-labeled dimercaptosuccinic acid scan, intravenous urography, and ultrasonography: A comparative study. The Journal of pediatrics, 120 (3): 399-403, 1992.

37- BAROLO L., GIGANTE Y., MAUTONE L., GHIRGA S., SOLOPERTO A., GIORGI A. and DI ANGELANTONIO S.: Ferritin Nanocage-Enabled Detection of Pathological Tau in Living Human Retinal Cells, 2024.

38- GUPTA S., JUNQUERA G.Y., NICASSIO L., BECKNELL B. and CHING C.B.: Trans IL-6 signaling does not appear to play a role in renal scarring after urinary tract infection. Journal of Pediatric Urology, 16 (5): 586-591, 2020.

39- SHEU J.N., CHEN M.C., CHEN S.M., CHEN S.L., CHIOU S.Y. and LUE K.H.: Relationship between serum and urine interleukin-6 elevations and renal scarring in children with acute pyelonephritis. Scandinavian journal of urology and nephrology, 43 (2): 133-137, 2009.

40- TAYLOR Jr., A.: Quantitation of renal function with static imaging agents.In Seminars in nuclear medicine (Vol. 12, No. 4, pp. 330-344). WB Saunders, 1982.

41- CAROLI A., REMUZZI A. and LERMAN L.O.: Basic principles and new advances in kidney imaging. Kidney international, 100 (5): 1001-1011, 2021.

42- LOEWEN J. and GREENBAUM L.A.: Imaging Kidneys and the Urinary Tract. In Pediatric Nephrology (pp. 173-211). Cham: Springer International Publishing, 2022.

دراسة در جة الارتباط بين انترلوكين -٦ البولى والمسح الذرى على الكلى فى الكشف عن الندبات الكلويه عند الاطفال المصابين باعتلال المسالك البولية الانسدادى

الخلفية: اعتلال الكلية الانسدادى هو أى مرض في المسالك البولية يتميز بضعف تدفق البول عبر المسالك والذى، إذا ترك دون علاج، سوف يسبب ندبات كلوية تدريجية. تمت دراسة إنترلوكين-٦على نطاق واسع لدى الأطفال الذين يعانون من اعتلال الكلية الانسدادى، مع التركيز على ارتباطه بالتندب الكلوى. وقد أظهرت الدراسات ارتفاع مستويات إنترلوكين-٦ لدى الأطفال الذين يعانون من تندب كلوى، مما يشير إلى إمكانية استخدامه كمؤشر حيوى لالتهاب الكلى وتندبها.

الهدف من العمل: تقييم العلاقة بين إنترلوكين-٦ البولية وفحص الكلى فى الكشف عن تندب الكلى لدى الأطفال المصابين باعتلال الكلية الانسدادى.

المرضى والطرق: هذه الدراسة هى دراسة حالة مراقبة. أجريت هذه الدراسة فى قسم أمراض كلى الأطفال بمستشفى الأطفال جامعة عين شمس. وكانت مدة الدراسة ٦ أشهر. كان مجتمع الدراسة ١٥ حالة تم قبولها من اعتلال الكلية الانسدادى المؤكد فى نوبة حادة من التهاب الحويضة والكلية و١٥ حالة صحية متطابقة. بالنسبة لجميع الحالات المسجلة، تم أخذ التاريخ الكامل بما فى ذلك العمر عند التشخيص وتقديم الشكوى عند القبول والتاريخ السابق للعمليات السابقة. تم إجراء الفحص السريرى الكامل، وإجراء الفحوصات المخبرية بما فى ذلك اختبارات وظائف الكلى، وتحليل البول، ومستوى إنترلوكين-٦ فى البول، والفحوصات الإشعاعية بما فى ذلك الموجات فوق الصوتية للحوض ومسح DMSA.

النتائج: كان متوسط عمر مجموعة الدراسة ٦ سنوات، وكان ٧٣٪ منهم ذكوراً دون أى فروق ذات دلالة إحصائية بين المجموعتين فى العمر أو الجنس. تم تشخيص معظم الحالات على أنها صمام إحليلى خلفى مع ارتجاع مثانى حالبى وموه الكلية الثنائى، وشملت التشخيصات الأخرى الارتجاع المثانى الحالبى الأولى والمثانة العصبية وحصوات الحالب. أظهرت دراستنا أن دراستنا بحثت فى العلاقة بين مستويات إنترلوكين-٦ البولية، ومسح الكلى DMSA، ودرجات مرض الكلى المزمن لدى الأطفال الذين يعانون من اعتلال الكلية الانسدادى. بينما وجدنا أن هناك زيادة ذات دلالة إحصائية فى الحالات مقارنة بالمجموعات الضابطة فيما يتعلق بمستوى إنترلوكين-٦ وأن المستوى انخفض بشكل ملحوظ بعد شفاء نوبة التهاب الحويضة والكلية ($p < ٠,٠٠١$)، إلا أننا لم نلاحظ وجود علاقة ذات دلالة إحصائية بين إنترلوكين-٦ مستويات ونتائج فحص الكلى DMSA. بالإضافة إلى ذلك، لم يكن هناك ارتباط كبير بين مستويات إنترلوكين-٦ والدرجات المختلفة لمرض الكلى المزمن.

الاستنتاج: تشير النتائج التى توصلنا إليها إلى أنه فى حين أن إنترلوكين-٦ البولى قد يكون بمثابة علامة على التهاب الكلى، فإنه قد لا يرتبط بشكل مباشر مع مدى تندب الكلى أو شدة مرض الكلى المزمن لدى مرضى الأطفال الذين يعانون من اعتلال الكلية الانسدادى. قد يوفر المزيد من البحث بأحجام عينات أكبر والمتابعة الطولية رؤى أعمق حول التفاعل المعقد بين المؤشرات الحيوية البولية، وطرائق التصوير، ووظيفة الكلى فى هذه الفئة من المرضى. بالإضافة إلى ذلك، فإن القيود المفروضة على عمليات فحص DMSA، بما فى ذلك التحديات التقنية وعدم الدقة المحتملة، تؤكد الحاجة إلى أساليب تشخيصية بديلة أو مساعدة فى تقييم التندب الكلوى.