Predictors of Renal Dysfunction in Adults with Childhood Vesicoureteral Reflux after Long-Term Follow-Up

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Abstract

BACKGROUND: Triad of childhood vesicoureteral reflux (VUR), urinary infection (UTI) and renal scarring might initiate potentially serious consequences that lead to renal dysfunction manifested at the second or third decade of life.

AIM: To identify the risk factors predictive for renal dysfunction in adults with primary VUR after long-term follow-up.

METHODS: We evaluated the records of 101 children (94.1% female, 5.9% male) at a median age of 5.2 ± 2.3 years (1-12 years), suffering from UTI and VUR. The patients were interviewed after mean 21 years from the first episodes of VUR (8 to 32 years). Renal function was determined from the estimated glomerular filtration rate (eGFR).

RESULTS: Renal scarring was detected in 68.3% out of 82 patients and bilateral one in 7.3% patients. Linear regression analysis revealed that presence of proteinuria (B = -33.7, p=0.0001), the greater number of years from VUR diagnosis (B = -1.6, p = 0.002) and renal scarring (B = -14.8, p = 0.005) appeared as independent predictors of reduced global eGFRcreat. The same variables plus microalbuminuria (B = -1.0, p = 0.012) appeared as independent predictors of reduced global eGFRcreat-cys. Bilateral scarring (OR=25.5, p = 0.003) appeared as independent predictor of greater risk for CKD assessed using eGFRcreat while greater number of years from VUR diagnosis (OR = 1.7, p = 0.092), microalbuminuria (OR = 1.3, p = 0.047) and again bilateral scarring (OR = 31.3, p = 0.040) appeared as predictors of risk for CKD assessed using eGFRcreat-cys.

CONCLUSION: Identification of those with an increased risk of progression to CKD should be the goal in all patients with childhood VUR. Their systematic follow-up should be till adulthood and older age.

Introduction

Primary vesicoureteral reflux (VUR) is a congenital urinary tract anomaly manifested by either a unilateral or bilateral reflux of urine from the bladder to the kidney which is diagnosed mostly after an episode of urinary tract infection (UTI) [1], [2]. The incidence of VUR is hard to establish but approximately affects 1-2% of children [3], and is much higher among children with UTI (15-70%, depending on age) [4]. The association between VUR and UTI with potentially serious consequences that ultimately lead to reflux nephropathy and renal dysfunction and/or failure in children is well established, from both clinical and experimental studies [5], [6], [7], [8]. Also, the association between VUR and the renal scarring has been confirmed in numerous published studies, and predictive risk factors for its occurrence have been established [8], [9], [10], [11], [12], [13], [14]. Furthermore, despite many advances have been made over the past decades in understanding the childhood VUR, its relations to UTI and prognosis as well as its choice of treatment, there have been still conflicting reports on the risk factors for worsening renal function in adult patients who were treated for childhood VUR.

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Methods

We evaluated the records of 101 children of both sexes, aged between one and 12 years, suffering from UTI and primary VUR. According to the availability at that time, VUR was diagnosed with direct radionuclide cystography (RNC) at the Institute of pathophysiology and nuclear medicine in the presence of pediatric nephrologist and the specialised nurse from University Children' Hospital. Patients with VUR associated with posterior urethral valves, ectopic ureterocele, neurogenic bladder, and other obstructive uropathies below bladder were excluded from the study.

The following clinical variables were obtained from patient record: gender, the age of diagnosis of primary VUR (years), grade of primary VUR, unilateral or bilateral primary VUR, history of UTI, treatment modality (medical, surgical or endoscopic). VUR was graded according to International Reflux Study Committee into five grades [1], [15], [16]. Renal scarring was detected with technetium-99 m labelled dimercaptosuccinic acid (DMSA) renal scintigraphy, which was performed within 6 months of UTI [17].

The patients were interviewed after 20,75 ± 6,46 years from the first episodes of VUR (minimum 8 to maximum 32 years). At the office visit, clinical history was taken. On physical examination weight and height as well as blood pressure were measured (systolic and diastolic). Also, blood and urine samples were collected for further analysis (concentration of creatinine and cystatin C in serum, albumin in urine and proteinuria using a dipstick) and ultrasonographic examination (measurements) of kidneys (Siemens Acusson S3000) was done. Creatinine clearance (CrCl) was calculated according to the Cockcroft-Gault Equation [18]. According to the recommendation of Kidney Disease Improving Global Outcomes (KDIGO) [19] renal function was determined from the estimated glomerular filtration rate (eGFR) using the CKD-EPI Creatinine Equation (2009) for eGFRcreat and 2012 CKD-EPI creatinine-cystatin C equation for eGFRcreat-cyst. In accordance with this recommendation [19] eGFR was categorized into 5 categories as follows: G1-normal or high ($\geq$ 90 ml/min/1.73 m^2), G2-mildly decreased (60-89 ml/min/1.73 m^2), G3a-mildly to moderately decreased (45-59 ml/min/1.73 m^2), G3b-moderately to severely decreased (30-44 ml/min/1.73 m^2), G4-severely decreased (15-29 ml/min/1.73 m^2) and G5-kidney failure (< 15 ml/min/1.73 m^2). Thus patients were stratified by eGFR into groups. Chronic kidney disease (CKD) was confirmed if eGFRcreat and/or eGFRcreat-cyst was < 60 ml/min/1.73 m^2 [19].

Statistical analysis

Categorical parameters were summarised as percentages and continuous parameters as mean ± SD. Comparisons between groups were performed using Student-t-test and ANOVA analysis of variance with Bonferroni post-hoc analysis for continuous parameters and Pearson's chi-square test for categorical parameters. Assessment of correlation of various echorenographic parameters was done using Pearson's correlation analysis. Multiple linear and logistic regression analyses were performed to determine independent predictors of reduced eGFR and/or CKD presence, respectively. The area under the receiver operating characteristics (ROC) curve (AUC) was performed to quantify the value of independent predictors in discrimination of patients with and without CKD. All data analysis was performed using SPSS version 25.0 (IBM SPSS, Inc., Chicago, Illinois) and p-value ≤ 0.05 was considered significant.

Results

The baseline characteristics of patients are summarised in Table 1. A total of 101 patients diagnosed with primary VUR were recruited, of which 95/94.1% were female and 6/5,9% male. The median age at VUR diagnosis was 5.2 ± 2.3 years. VUR was diagnosed at one year in 2 patients, at two years in 10 patients, at 3 years in 9 patients, at 4 years in 19 patients, at 5 years in 12 patients, at 6 years in 18 patients, at 7 years in 16 patients, at 8 years in 9 patients, at 10 years in 2 patients, at 11 years in 3 patients and at 12 years in one patient. In all patients fever and UTI was present before VUR diagnosis was established. VUR was diagnosed at right kidney in 63 patients and left kidney in 74 patients. Among patients with unilateral VUR, 48/76.2% had low-grade VUR (i.e. I–III) at right kidney and 61/82.4% at left kidney, while high-grade VUR (i.e. IV–V) was present in 15/23.8% patients at right kidney and 13/17.6% patients at left kidney. Among those with bilateral VUR, 37 had a low-grade VUR, and 49 had a high-grade VUR. Most patients (94.0%) were administrated prophylactic antibiotics, and the rest of all (7.0%) have STING (subureteral Teflon injection) procedure. In one patient nephrectomy of the right kidney was done.

Of the 101 patients, 82 had a record of undergoing a DMSA within the time of VUR diagnosis. Considering both the right and left kidney, renal scarring was detected in 56/68.3% out of 82 patients

and bilateral one in 6/7.3% patients (Table 1).

Table 1: Baseline characteristics of patients

Parameters	Numbers (%)	
Gender (n/%)		
Female	95/94.1	
Male	6/5.9	
Age at onset of VUR (years)		
Mean	5.2 ± 2.3	
Range	1 to 12	
1-2 years (n/%)	12/11.9	
2-5 years (n/%)	40/39.6	
> 5 years (n/%)	49/48.5	
UTI (n/%)	101/100	
Treatment		
Antibiotics	94/94.0	
STING	7/7.0	
Nephrectomy	1/0.9	
VUR grade	Right kidney (n = 63)	Left kidney (n = 74)
	2.89 ± 0.80	2.70 ± 0.75
Grade II (n/%)	23/36.5	35/47,3
Grade III (n/%)	25/39.7	26/35,1
Grade IV (n/%)	14/22.2	13/17,6
Grade V (n/%)	1/1.6	-
Bilateral VUR* (n/%)	37/37	
Renal scaring** (n/%)	56/68.3	
Bilateral scaring**	6/7.3	

* For 100 patients; ** For 82 patients; VUR = vesicoureteral reflux; STING = subureteral teflon injection

After mean 20.8 ± 6.5 years from the first episode of VUR (8 to 32 years), laboratory analysis (serum, urine and ultrasound) were done. Patients who were 26.1 ± 4.9 of age (17 to 36 years) were divided according to the value of eGFRcreat into 3 categories of renal dysfunction and compared regarding characteristics considered of importance for renal function. Due to the small number of patients, 3Ga and 3Gb were considered as one group. Out of all, 67/66.3% were with normal renal function (G1), 27/26.7% were with mildly decreased (G2), and 7/6.9% were with moderately decreased (G3) renal function. The results of the comparison are shown in Table 2.

A comparison of the characteristics among patients stratified according to the eGFRcreat (Table 2) revealed that those with moderately impaired renal function in comparison to those with normal function were older, diagnosed with VUR at a younger age with significantly more years passed by after VUR was diagnosed, had a more serious grade of VUR (especially for left kidney) along with more frequently bilateral one. Of note was that renal scarrings were significantly more frequently present in the same patients' group while bilateral one was significantly absent in patients with normal renal function in comparison to those with some grade of dysfunction. Blood pressure measurements didn't show any difference between the groups. Furthermore, patients with mildly and moderately impaired renal function compared to those that had normal function showed a significantly lower value of CrCl. Those with moderately impaired renal function also showed ultrasonographical measured the significantly smaller size of both kidneys, a higher percentage of proteinuria as well as the higher value of albuminuria in comparison to those with normal function (Table 2). When the same comparison was made according to the value of eGFRcreat-cys, we obtained almost identical results.

Table 2: Comparison of clinical and laboratory finding in adult patients who were diagnosed with childhood VUR divided according to the categories of eGFRcreat

Characteristics	eGFRcreat (ml/min/1.73 m^2)			p
	G1 = ≥ 90 (n = 67)	G2 = 60-89 (n = 27)	G3 = 30-59 (n = 7)	
Age (years)	24.8 ± 5.0	28.5 ± 3.5	29.0 ± 4.3	0.001
Gender (%)				
male	6/9.0	0	0	P = 0.197
female	61/91.0	27/100	7/100	
Age of VUR diagnosis (years)	5.1 ± 2.4	5.8 ± 2.2	4.5 ± 1.4	0.293
Time from the first episode of VUR (years)	19.6 ± 4.5	22.6 ± 4.0	24.4 ± 3.6	0.001
VUR grade/right kidney	(n = 40)	(n = 17)	(n = 6)	0.324
	2.7 ± 0.7	3.1 ± 0.9	3.0 ± 0.8	
VUR grade/left kidney	(n = 48)	(n = 21)	(n = 5)	0.008
	2.5 ± 0.6	2.9 ± 0.8	3.4 ± 0.8	
VUR bilateral				
no	44/66.7	16/59.3	3/42.9	0.415
yes	22/33.3	11/40.7	4/57.1	
Treatment(%)				0.173
antibiotics	64/95.5	23/85.2	7/100	
STING	3/ 4.5	4/14.8	0	
Scarring (%) (n=82)				0.051
no	22/40.7	3/14.3	1/14.3	
yes	32/59.3	18/85.7	6/85.7	
Bilateral scarring (%) (n=82)				0.001
no	51/94.4	21/100	4/57.1	
yes	1/50.0	0	3/42.9	
BPs (mmHg)	115.9 ± 9.4	116.6 ± 8.1	113.8 ± 11.6	0.772
BPd (mmHg)	76.9 ± 6.0	77.7 ± 4.5	77.8 ± 4.0	0.765
Right kidney (mm)	84.5 ± 14.4	91.3 ± 11.9	76.4 ± 16.3	0.022
Left kidney (mm)	84.0 ± 16.2	89.4 ± 13.0	72.1 ± 14.2	0.027
CrCl (ml/min)	118.9 ± 26.9	77.9 ± 12.6	55.2 ± 14.4	0.0001
Proteinuria (n/%)				0.0001
no	64/95.5	23/85.2	0	
yes	3/4.5	4/14.8	7/100	
Albuminuria (mg/L)	11.2 ± 4.2	13.6 ± 6.2	14.4 ± 1.5	0.038

eGFRcreat = glomerular filtration rate according serum creatinine concentration; VUR = vesicoureteral reflux; STING = subureteral teflon injection; BPs = blood pressure in systole; BPd = blood pressure in diastole; CrCl = creatinin clearence.

In addition, correlation of either eGFRcreat or eGFRcreat-cys with parameters that were related revealed significant relation between lower eGFRcreat or eGFRcreat-cys and longer time since VUR diagnosis (r = -0.450, p = 0.0001; r = -0.445, p = 0.0001; respectively), higher grade of primary unilateral VUR (r = -0.352, p = 0.002; r = -0.324, p = 0.005; respectively), presence of unilateral renal scarring (r = -0.244, p = 0.027; r = -0.294, p = 0.007; respectively) and bilateral ones (r = -0.307, p = 0.005; r = -0.329, p = 0.003; respectively) as well as presence of proteinuria (r = -0.486, p = 0.0001; r = -0.463, p = 0.0001; respectively) and greater level of albuminuria (r = -0.251, p = 0.012; r = -0.307, p = 0.002; respectively).

Predictive variables of reduced eGFR

To determine the independent predictors of reduced eGFR among patients with childhood VUR, we performed multiple stepwise linear regression analysis with covariates that showed a significant relation to it. The results demonstrated that the presence of proteinuria, the greater number of years since from VUR diagnosis and the presence of renal scarring appeared as independent predictors of reduced global eGFR assessed according to serum creatinine value (eGFRcreat) (Model 1, Table 3, Figure 1). Microalbuminuria (B = −0.159, p = 0.117), bilateral renal scarring (−0.088, p = 0.382) and VUR grade of left kidney (B = −0.082, p = 0.434) were

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excluded as non-predictive variables in the regression analysis. When we used eGFR assessed according to serum creatinine and cystatin C values (eGFRcreat-cys) the results demonstrated that the presence of proteinuria, value of microalbuminuria, the greater number of years since VUR diagnosis and the presence of renal scarring appeared as independent predictors of reduced global eGFRcreat-cys (Model 2, Table 3, Figure 1).

Table 3: Multiple linear or logistic regression models of eGFR as the dependent variable and its independent predictors

Linear regression	B	Beta	Sig.	95%CI
Model 1				
Proteinuria	-33.783	-0.481	0.0001	(-47.387)-(-20.178)
Years VUR dgn	-1.651	-0.307	0.002	(-2.675) – (-0.628)
Renal scarring	-14.835	-0.274	0.005	(-24.973)-(-4.697)
Model 2				
Proteinuria	-33.031	0.522	0.0001	(-44.540)-(-21.521)
Years VUR dgn	-1.177	-0.243	0.005	(-1.991)-(-0.364)
Microalbuminuria	-1.027	-0.230	0.012	(-1.821)-(-0.233)
Renal scarring	-9.888	-0.203	0.018	(-18.032)-(-1.744)
Logistic regression	Exp(B)	Wald	Sig.	95%CI
Model 3				
Bilateral scarring	25.500	8.842	0.003	3.016-215.594
Model 4				
Years VUR dgn	1.769	3.998	0.092	0.911-3.436
Microalbuminuria	1.333	3.946	0.047	1.004-1.771
Bilateral scarring	31.304	4.233	0.040	1.177-832.313

Model 1: linear regression analysis with eGFRcreat as dependent variable; Model 2: linear regression analysis with eGFRcreat-cys as dependent variable; Model 3: logistic regression analysis with eGFRcreat with and without value of < 60 ml/min/1.73 m^2 as dependent variable. Model 4: logistic regression analysis with eGFRcreat-cys with and without value of < 60 ml/min/1.73 m^2 as dependent variable; CI = confidence interval; VUR = vesicoureteral reflux; Dgn = diagnosis.

Again bilateral renal scarring (−0.086, p = 0.330) and VUR grade of left kidney (B = −0.030, p = 0.742) were excluded as non-predictive variables in the regression analysis. To confirm the role of the same variables in the prediction of the presence of CKD (< 60 ml/min/1.73 m^2) we performed a logistic regression analysis using almost the same variables (proteinuria was excluded as an indisputable significant predictor) as independent predictors.
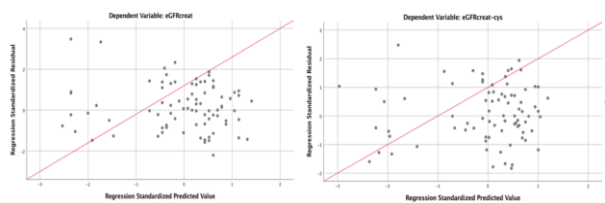

Figure 1: Scatter plot of standardised residual vs standardised predicted value with a regression line for eGFRcreat (left) and eGFRcreat-cys (right)

The results showed that only presence of bilateral scarring appeared as an independent predictor of risk for CKD (Model 3, Table 3) assessed using eGFRcreat. Years of VUR diagnosis (2,206, p = 0.137), VUR grade of left kidney (0.780, p = 0.337), microalbuminuria (0.106, p = 0.745) and renal scarring (0.161, p = 0.281) were excluded as non-predictive variables in the regression analysis. When we used eGFRcreat-cys, the greater number of years since VUR diagnosis, the value of microalbuminuria and presence of bilateral scarring appeared as predictors of risk for CKD (Model 4, Table 3). VUR grade of left

kidney (2.798, p = 0.094) and renal scarring (0.578, p = 0.447) were excluded as non-predictive variables in the regression analysis.

In order to confirm the role of independent predictors in discrimination of patients with and without CKD assessed using eGFRcreat-cys, ROC analysis (Figure 2) revealed that addition of microalbuminuria to bilateral scarring (AUC=0.667, 95% CI: 0.435-0.899, p = 0.123) and greater years since diagnosis VUR (AUC = 0.789, 95% CI: 0.660-0.919, p = 0.007) significantly improved the AUC (AUC = 0.809, 95% CI: 0.657–0.962, p = 0.004). Also, we determined 21.5 years since VUR diagnosis as a cut-off value with the highest sensitivity of 87.5% and a specificity of 57.5% for determining the existence of CKD according to eGFRcreat- cys.
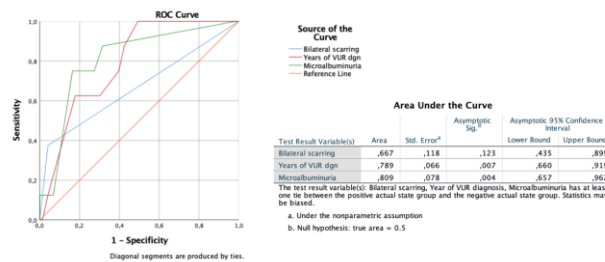
Figure 2: ROC curve for the presence of chronic kidney disease assessed using eGFRcreat-cys

Discussion

In the present study, a total of 101 patients were diagnosed with primary VUR at a median age of 5 years. Among patients with unilateral VUR, low-grade VUR (i.e. I–III) was present in over 70% of patients while high-grade VUR (i.e. IV–V) was present in 23.8% patients at right kidney and 17.6% patients at left kidney. Considering both the right and left kidney, renal scarring was detected in 56/68.3% out of 82 patients and bilateral one in 6/7.3% patients.

As we already stressed an association between childhood VUR and the renal scarring had been confirmed in numerous published studies [8], [9], [10], [11], [12], [13], [14]. In the meta-analysis of Shaikh et al., [12] the prevalence of renal scarring was 2.6 times (95% CI: 1.7–3.9) higher among children with VUR than among children without VUR (41% vs 17%; P < 001). Prospective clinical studies showed that the risk of renal scarring after acute DMSA abnormalities detected at acute febrile UTI is significantly greater in patients with high-grade VUR, affecting up to 89% with grade IV–V VUR [8], [20], [21]. In the meta-analysis of 27 clinical studies, Faust et al., [11] demonstrated an increased risk of acquired renal scarring in children with VUR *vs* without VUR

(OR 2.8 and 3.7, respectively).

Hence, the prevalence of renal scarring has been reported to be in the range from 15-62%. Bailey et al., [22] showed that after a mean of 24 years of follow-up out of 21 patients only 4/19% had normal kidneys, although the study included only those with gross childhood VUR. Also, Olbing et al., [23] in a prospective trial of 223 patients with severe VUR who were followed-up for 10 years showed unscarred kidneys on urography only in 38% of these children. Smellie et al., [24] found scars in 44% of their patients with severe VUR that were a follow-up for 10-41 years. Also, Vasama-Lahdes et al., in the study of 127 patients treated for non-obstructive VUR of any grade with the mean age of 41 years documented presence of unilateral scarring in 35% and bilateral one in 24% of subjects assessed by ultrasound.

Furthermore, Swerkersson et al., [8] in their retrospective analysis of 303 children younger than 2 years with a culture verified UTI and VUR in 22% of them, reported 26% permanent renal damage according to DMSA scintigraphy. Recently, among 958 patients studied by Madani et al., [25] DMSA scan showed renal damage in 41.2% of patients. Almost all published data found a strong association between severity of VUR and renal scarring. However, our study showed a higher percentage of renal scarring which was in line with the study of Abeysekara et al., [26] and Macedo et al., [27] who detected renal scarring among patients with primary VUR in 55.3% and 55.2% of them, respectively. The higher percentages probably should be explained by ineffective treatment of UTI and VUR in that period when patients were diagnosed along with the fact that patients might have had multiple febrile UTIs before their first cystography. Furthermore, the higher percentage of renal scarring was also found when DMSA scan was used instead of ultrasound for detection.

Given that renal scarring was recognised as a predictive factor for an increased risk of renal dysfunction that may not be present until the second or third decade of life, it was of great importance to conduct our study to confirm such findings [1]. Thus, in our study of patients with unilateral or bilateral childhood primary VUR it was found that patients with moderately impaired renal function in comparison to those with normal function stratified according to the eGFRcreat or eGFRcreat-cys were older, diagnosed with VUR at a younger age with significantly more years passed by after VUR was diagnosed, had a more serious grade of VUR (especially for left kidney) along with more frequently bilateral one. Also, renal scarring was more frequently present in patients with renal dysfunction while bilateral one was significantly absent in patients with normal renal function in comparison to those with some grade of dysfunction. As for predictors of renal dysfunction regression analysis revealed that presence of proteinuria, the greater number of years since VUR diagnosis and the

presence of renal scarring appeared as independent predictors of reduced global eGFRcreat while the same variables plus microalbuminuria appeared as independent predictors of reduced global eGFRcreat-cys. Furthermore, presence of bilateral scarring appeared as an independent predictor of greater risk for CKD assessed using eGFRcreat while a greater number of years since VUR diagnosis, the value of microalbuminuria and again the presence of bilateral scarring appeared as predictors of risk for CKD assessed using eGFRcreat-cys.

Our results were in general in line with those from literature. Several studies have focused on risk factors for developing renal dysfunction and/or CKD in patients with childhood VUR. Ardissino et al., [28] in the epidemiological study conducted in Italy (i.e. ItalKid Project), documented that VUR was found to be the single leading cause of CKD in children, accounting for 25.8% of cases. When the population was subdivided according to the creatinine clearance (Ccr) levels, patients with VUR and Ccr < 25 mL/min/1.73 m^2 had an overall risk of 68% for progressing to end-stage renal disease (ESRD) by the age of 20. In the study of El-Khatib et al., [29] 147 patients with reflux nephropathy and/or primary VUR were followed for two years or more (range 2-19 years) and deterioration in renal function was documented in 37% of them; the identified risk factors were the presence of proteinuria, an elevated plasma creatinine concentration, bilateral scarring, male sex and the presence of hypertension. Nakashima et al., [30], followed 95 patients who had a renal scar or grade III or higher VUR and found that 35% demonstrated renal function deterioration; the identified risk factors were the presence of bilateral scarring, proteinuria > 300 mg per day, diastolic hypertension and low eGFR. In addition, Vasama-Lahdes et al., [9] in 147 (55%) of 267 patients treated for childhood VUR found that eGFR was normal only in 33% of patients and those with bilateral scarring (3%) were significantly more likely to have reduced eGFR, while approximately 7% of patients with VUR progress to ESRD. Caione et al., [31] followed-up for 1-16 years 50 patients with bilateral VUR and found CKD in 54% of them with significant risk for its development in those with bilateral high-grade VUR and serum creatinine levels > 6.0 mg/L in the first year of life. However, Silva et al., [32] determined that age at diagnosis > 24 months, VUR grade V, bilateral renal damage, and a delay in the diagnosis of VUR of > 12 months after UTI were independent predictors of CKD. In addition, North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) Registry found that in only 8.5% of patients VUR was the cause of CKD whereas Novak et al., [33] on data from the NAPRTCS suggested that older age, higher CKD stage, and history of UTI are significant risk factors for CKD progression in children with VUR. Furthermore, Chen at al., [34] recruited total of 173 patients with primary VUR and found that older age of VUR diagnosis (≥ 5 years vs < 1 year), higher grade of

VUR and higher number of UTI were risk factors for renal scarring, whereas a younger age of VUR diagnosis, renal scarring and acute pyelonephritis were risk factors for developing CKD stage two or higher.

Study limitations: The main limitation of our study was a relatively small number of patients. Also, the number of repetitive UTI during a follow-up period was not documented. We didn't analyse either biochemical parameters of renal function in the childhood or the aetiology of infection.

In conclusion, in adult patients who were treated for childhood VUR, the presence of proteinuria, the greater number of years since VUR diagnosis and renal scarring appeared as independent predictors of reduced global eGFRcreat along with microalbuminuria for reduced eGFRcreat-cys. Bilateral scarring appeared as an independent predictor of greater risk for CKD assessed either using eGFRcreat or eGFRcreat-cys.

A better understanding of the risk factors for renal scarring, and deteriorating renal function can be useful in tailoring the management and therapeutic approach for VUR. Additionally, identification of those with an increased risk of progression to CKD should be the goal in all patients with childhood VUR. Their systematic follow-up should be till adulthood and further to an older age.

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