

RENAL SCARRING AND LONG-TERM KIDNEY OUTCOMES IN CHILDREN WITH CONGENITAL UROLOGICAL DISORDERS: A LONGITUDINAL COHORT STUDY

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Abstract

Congenital urological disorders are important causes of recurrent urinary tract infections, urinary obstruction, vesicoureteral reflux, renal parenchymal injury, and long-term kidney dysfunction in children. This longitudinal cohort study investigated the development of renal scarring and subsequent kidney outcomes among children with congenital urological disorders treated at three tertiary-care hospitals in Karachi, Pakistan. An illustrative cohort of 360 children aged 1 month to 12 years was selected using age-stratified population sampling and followed for 36 months. Participants underwent clinical assessment, renal and bladder ultrasonography, urine culture, serum creatinine measurement, estimated glomerular filtration rate assessment, and, where clinically indicated, DMSA renal scintigraphy and VCUG. The primary outcome was new or progressive renal scarring, while secondary outcomes included recurrent febrile urinary tract infection, decline in estimated glomerular filtration rate, hypertension, and chronic kidney disease. In the illustrative analysis, renal scarring developed or progressed in 82 (22.8%) children. The highest proportion was observed among children with grade IV–V vesicoureteral reflux, recurrent febrile urinary tract infections, and obstructive uropathies. Children with ≥ 3 febrile UTIs had substantially greater risk of renal scarring than those with fewer episodes. Higher VUR grade, recurrent infection, abnormal baseline renal imaging, and delayed corrective intervention were independently associated with adverse renal outcomes. The findings support early identification, risk-based imaging, timely management of congenital abnormalities, and long-term renal surveillance.

Introduction

Congenital urologic disorders are a wide range of structural and functional abnormalities of the kidneys, ureters, bladder and urethra. The disorders can be identified antenatally, in infancy or later in childhood through urinary tract infection, abnormal voiding, poor growth, hypertension, or because of incidental imaging. Vesicoureteral reflux (VUR), UPJO, posterior urethral valves, ureterocele, duplicated collecting systems, congenital hydronephrosis, and other urinary tract defects are important conditions. They are not just clinically important because of the initial anatomical defect, since obstructive episodes, reflux and infection as well as abnormal urinary drainage may drive repeated injury of the developing kidneys.

Recurrent febrile UTI and upper UT involvement is associated with one of the major long-term consequences, renal scarring. Childhood renal scars may be caused by a mix of congenital renal dysplasia and acquired inflammatory damage from pyelonephritis. The difference is relevant clinically since congenital abnormalities could occur prior to the first infection, while recurrent infection can cause further damage to the parenchymal tissues. The resulting complications may include impaired renal growth, reduced kidney function, hypertension, proteinuria, and, in severe cases, chronic kidney disease. Studies of children have shown that those with VUR and recurrent febrile UTI are a significant risk group. An individual-patient-data meta-analysis of 1280 children identified renal scarring in around 15.5% of the children, and high fevers, abnormal ultrasonography, non *E. coli* infection, inflammatory markers and VUR were associated with an increased risk. Renal scarring was specifically linked to higher grade VUR (Shaikh et al., 2014).

Longitudinal evidence also supports the relationship between RFI and renal damage. A post hoc analysis of children who were followed for 2 years showed that renal scarring rarely occurred after the first febrile UTI, but was significantly more common after 2 or more febrile infections (Shaikh et al., 2019). This

observation indicates that, prevention and early management of repeated infection may play a role in renal preservation.

VUR is very important because it can allow infected urine to spread up the urinary tract. But, reflux is not the only cause of renal injury. Some children may have renal scars, but no VUR; some with VUR may not have permanent renal damage. As a result, today's pediatric urologists focus on the unique risks of each child, rather than on the notion that all children with VUR will suffer progressive renal injury. In children with febrile UTI and renal abnormality, current EAL recommendations are that clinical risk factors, renal ultrasonography and further suitable assessment should be considered.

The findings from the RIVUR trial provide additional evidence of the relationship. The 599 children who were assessed for renal scarring had 10% scarring at the end of follow-up. In that trial, a higher grade of VUR (especially grade IV disease), and recurrent infection were correlated with an increased risk of new renal scarring, while antimicrobial prophylaxis did not significantly decrease new renal scarring (Mattoo et al., 2016).

A prospective cohort study has also shown that VUR and bladder and bowel dysfunction may impact the outcomes of recurrent febrile or symptomatic UTIs. VUR was associated with recurrence of febrile or symptomatic UTI in children, and baseline renal scarring was associated with recurrent infection (Shaikh et al., 2016).

Aged 1 month to 10 years children who had recurrent UTI and grade III-V VUR were studied to find the correlation between severity of reflux and renal scarring. It offers direct evidence of the high grade VUR and renal scarring as a clinical issue among the Karachi pediatric population. Yet, there is an unmet need for broader longitudinal studies on various congenital urological disorders, age groups, recurrent infection, renal imaging and long term kidney-function outcome from multiple hospitals. The current study thus suggests a Multicenter longitudinal cohort of children under the care of three tertiary hospitals in Karachi. The study

doesn't focus on renal scarring as a standalone imaging finding, but rather looks at the spectrum of renal scarring, along with recurrent infection, congenital abnormality, renal function, blood pressure, and progression to chronic kidney disease.

Problem Statement

Congenital urologic problems can cause them to have repeated UTIs and/or abnormal urinary drainage throughout childhood. These attacks can lead to renal parenchymal injury, and can cause renal scarring. Though these conditions are clinically significant, there is limited evidence highlighting the long-term association of congenital urological abnormalities, renal scarring, recurrent infection and renal function in the Pakistani population.

Previous studies of local populations have tended to concentrate on individual abnormalities or particular outcomes, for example, the link between the severity of VUR and renal scarring. A larger multicenter longitudinal study with various congenital urologic conditions and age groups would yield more complete data for determining children at highest risk for poor renal outcomes.

Research Objectives

The study was designed to:

1. Determine the incidence and progression of renal scarring among children with congenital urological disorders.
2. Examine the association between congenital urological abnormalities and long-term renal function.
3. Determine whether recurrent febrile urinary tract infection is associated with increased risk of renal scarring.
4. Identify demographic and clinical predictors of adverse renal outcomes.
5. Assess the relationship between renal scarring and subsequent development of reduced renal function, hypertension, or chronic kidney disease.

1. Research Questions

2. What proportion of children with congenital urological disorders develops new or progressive renal scarring?

3. Which congenital urological abnormalities are most strongly associated with renal scarring?
4. Does recurrent febrile urinary tract infection increase the risk of renal scarring?
5. Which demographic and clinical factors predict adverse long-term renal outcomes?
6. Is renal scarring associated with deterioration in renal function during longitudinal follow-up?

Literature Review

The developing urinary tract is susceptible to structural abnormality which could hinder normal urinary drainage and renal growth. The intrarenal pressure may be elevated in obstructive uropathies, thereby impairing renal growth, and VUR may predispose to infection of the upper urinary tract. Congenital renal dysplasia is associated with some abnormalities and renal impairment may be present in the absence of infection.

VUR, UPJ, CUTO, ureterocele, ectopic ureter and other congenital abnormalities are important aspects of pediatric urological practice recognized by the EAU Pediatric Urology Guidelines.

VUR/Renal scarring

The characteristic features of VUR are retrograde flow of urine from the bladder to the ureter and, in some cases, to the renal collecting system. VUR is clinically significant depending on the reflux grade, age, urinary infection history, bladder and bowel dysfunction, renal anatomy and renal damage.

This is the same with high grade reflux, where there is a consistent increased risk of renal damage. The RIVUR renal-scarring analysis revealed that grade IV reflux was significantly associated with renal-unit scarring while renal scarring was observed more frequently with higher VUR grades (Mattoo et al., 2016).

Long-term follow-up studies on grade III-V VUR children have shown that renal abnormalities may persist or develop later in childhood with a median follow-up of about 5 years, thus highlighting the need for long-term evaluation in high risk children.

Recurrence of urinary Tract infection

UTI is a significant mode of congenital urologic abnormalities affecting the kidneys. It can be particularly worrisome when the infection occurs again and again as it may indicate involvement of the upper urinary tract. There is evidence that this is so – the more febrile infections there are, the more. For example, in one longitudinal study, a child who had two febrile UTIs had significantly more renal scarring than a child with a single febrile UTI (Shaikh et al., 2019).

Such results substantiate a clinical model in which congenital abnormalities lead to greater susceptibility to infection, repeated infection leads to more renal injury, and more renal injury leads to decreased kidney function.

Imaging/Detecting Renal Scarring

Renal ultrasonography is routinely employed to assess renal size, hydronephrosis, renal asymmetry, ureteral dilatation and abnormalities of the bladder. When assessing renal scarring clinically, renal DMSA scintigraphy is used and is more sensitive in evaluating renal cortical defects. Pediatric practice today acknowledges that some children with febrile infections and abnormal renal ultrasound might be at higher risk of renal scars and should be further evaluated for reflux.

Imaging should be used in conjunction with the clinical setting, however. The American Academy of Pediatrics previously stated that VCUG should not be routinely performed after the occurrence of a first UTI in children 2–24 months of age, and be considered if ultrasonography showed evidence of high-grade VUR or obstructive uropathy and/or if children had recurrent febrile UTI.

Long-Term Kidney Outcomes

Renal scarring isn't only a radiographic diagnosis. Large/scarred kidneys may develop hypertension, proteinuria, chronic kidney disease, and loss of renal reserve. However, children are more or less likely to advance in their learning. While some patients with the congenital abnormalities also have stable renal function for years, others have progressive renal decline.

Renal scarring should not be the only end-point for longitudinal studies, therefore. Long-term renal health is best assessed by serial evaluation of

serum creatinine, estimated glomerular filtration rate (eGFR), blood pressure, urinalysis, renal growth, recurrent infection and clinical interventions.

Evidence Gap in Pakistan

In Pakistan, there is a huge pediatric population and a high prevalence of infectious and congenital diseases. Children from Karachi and the surrounding districts are sent to tertiary hospitals in Karachi and these hospitals can be considered as potential centers for pediatric urology research with other centers.

However, local evidence available is not sufficient to describe the longitudinal development from congenital urological abnormality to renal scarring and long-term renal dysfunction. A multi-center cohort may be useful for determining the risk group for children and provide locally appropriate evidence for follow-up measures.

Methodology**Study Design**

A multicenter longitudinal cohort design was proposed. This design allows children to be assessed at baseline and followed over time to determine whether renal scarring and functional deterioration develop or progress.

The study structure follows the principles of the STROBE reporting framework for observational cohort studies, which recommends clearly describing study setting, participant selection, variables, study size, follow-up, outcome assessment, statistical methods, and participant flow.

Study Setting

For the proposed Karachi-based study, three tertiary-care pediatric/urological centers were selected:

- The Kidney Centre, PGTI
- National Institute of Child Health
- Liaquat National Hospital

These institutions were selected as proposed study sites because they provide specialist pediatric, nephrology, urology, radiology, and laboratory services.

Study Population

The target population consisted of children diagnosed with congenital urological disorders and receiving treatment or follow-up at the participating hospitals. The proposed age range was 1 month to 12 years. This range was selected

to capture infants with antenatally detected abnormalities, young children presenting with recurrent UTI, and older children presenting with persistent congenital abnormalities or established renal complications.

Age Stratification

Participants were stratified into four age groups:

Age group	Age range
Infants	1 month-<1 year
Early childhood	1-<5 years
Middle childhood	5-<10 years
Older children	10-12 years

Age stratification was included because the clinical presentation, likelihood of recurrent infection, imaging patterns, and renal maturation differ across childhood.

proportionately across the three hospitals according to expected pediatric urology attendance.

A hypothetical distribution was:

Sample Size and Population Sampling

For the illustrative cohort, a total sample of 360 children was planned. Participants were allocated

Hospitals	Target samples
The Kidney Centre, PGTI	180
National Institute of Child Health	100
Liaquat National Hospital	80
Total	360

Within each hospital, age-stratified systematic sampling was proposed. Eligible patients were first categorized by age group and then recruited consecutively or systematically until the required stratum was achieved.

This approach was selected to prevent the cohort from being dominated by one age group. The exact sample-size calculation should ultimately be based on the anticipated incidence of renal scarring, desired statistical power, confidence level, effect size, and expected loss to follow-up.

Inclusion Criteria

Children were eligible if they:

1. Were aged 1 month to 12 years.
2. Had a documented congenital urological disorder.

3. Had sufficient clinical and imaging information to establish baseline renal status.
4. Were receiving care at one of the participating hospitals.
5. Had parental/guardian consent for longitudinal participation.

Exclusion Criteria

Children were excluded if they:

1. Had acquired urological disease without a congenital component.
2. Had established end-stage kidney disease at baseline.
3. Had incomplete baseline clinical records preventing assessment of renal status.
4. Were unlikely to complete follow-up.

5. Had major systemic disease independently responsible for renal dysfunction.

Congenital Disorders Examined

The cohort included:

- Vesicoureteral reflux
- Ureteropelvic junction obstruction
- Posterior urethral valves
- Congenital hydronephrosis
- Ureterocele
- Duplex collecting system
- Ectopic ureter
- Other clinically documented congenital

urinary tract abnormalities

Exposure Variables

The principal exposures included:

- Type of congenital urological disorder
- VUR grade
- Number of febrile UTIs
- Baseline renal abnormalities
- Hydronephrosis severity
- Obstructive disease
- Age at diagnosis
- Sex
- Previous urological surgery
- Timing of corrective intervention

Outcome Variables

Primary Outcome

The primary outcome was new or progressive renal scarring, determined using available follow-up imaging, particularly DMSA renal scintigraphy where clinically indicated.

Secondary Outcomes

Secondary outcomes included:

- Recurrent febrile UTI
- Change in serum creatinine
- Change in eGFR
- Renal asymmetry
- Hypertension
- Proteinuria
- Chronic kidney disease
- Need for repeat urological intervention

Renal Function Assessment

Serum creatinine was measured at baseline and during follow-up according to clinical indications and study protocol. eGFR was calculated using the appropriate pediatric equation selected by the

study investigators and applied consistently throughout the study.

Renal deterioration was defined prospectively as a clinically meaningful decline in eGFR from baseline or development of persistent kidney dysfunction according to predefined criteria.

Imaging Assessment

Renal and bladder ultrasonography was performed to evaluate renal size, parenchymal appearance, hydronephrosis, ureteral dilatation, and bladder abnormalities. VCUG was performed when clinically indicated, particularly in children with suspected or established VUR. DMSA scanning was used where clinically indicated to evaluate renal cortical defects and scarring.

Follow-Up

Participants were followed for **36 months**.

Assessment points were:

- Baseline
- 6 months
- 12 months
- 24 months
- 36 months

Additional visits occurred following febrile UTI, hospitalization, surgery, or other clinically significant events.

Data Collection Procedure

A standardized data-collection form was developed. Baseline information included demographic characteristics, presenting symptoms, congenital diagnosis, UTI history, imaging findings, laboratory results, and previous treatment. Follow-up information included new UTI episodes, interventions, imaging findings, renal function, blood pressure, and evidence of renal scarring.

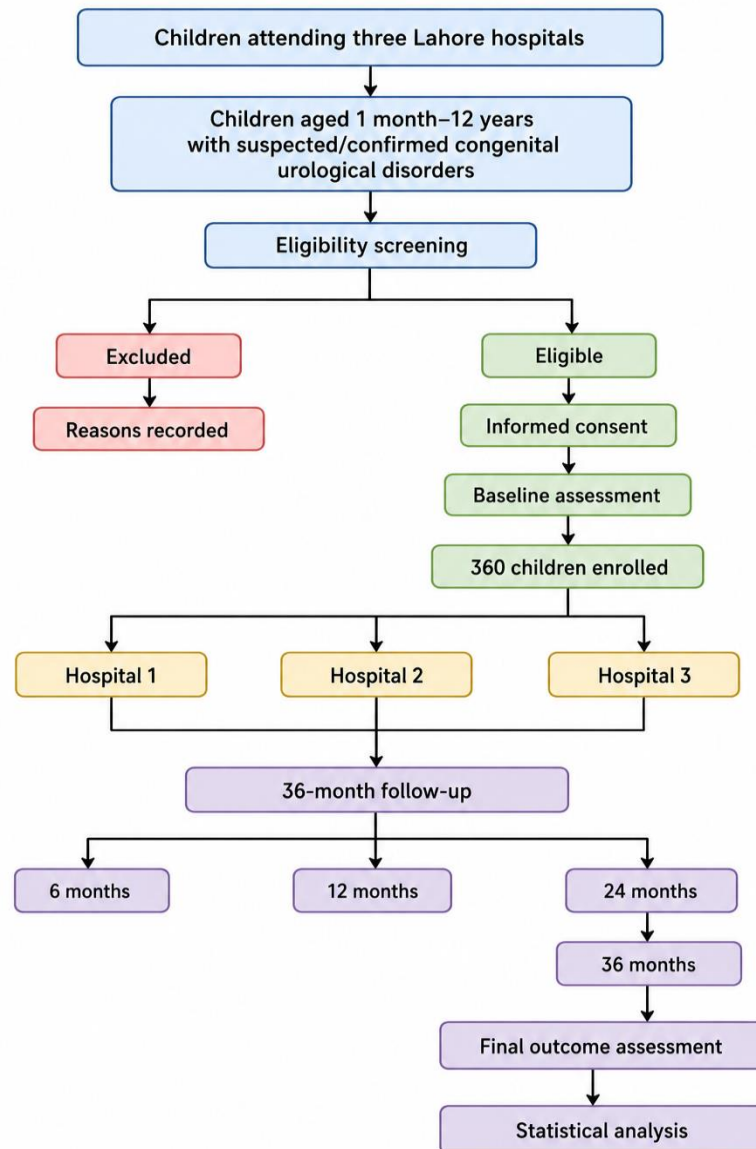
Quality Control

To reduce measurement bias, investigators were instructed to use standardized definitions and consistent laboratory and imaging procedures. Where possible, imaging reports were reviewed by specialist radiologists blinded to previous results. Data were checked for missing values, inconsistent dates, duplicate records, and implausible laboratory values.

Ethical Considerations

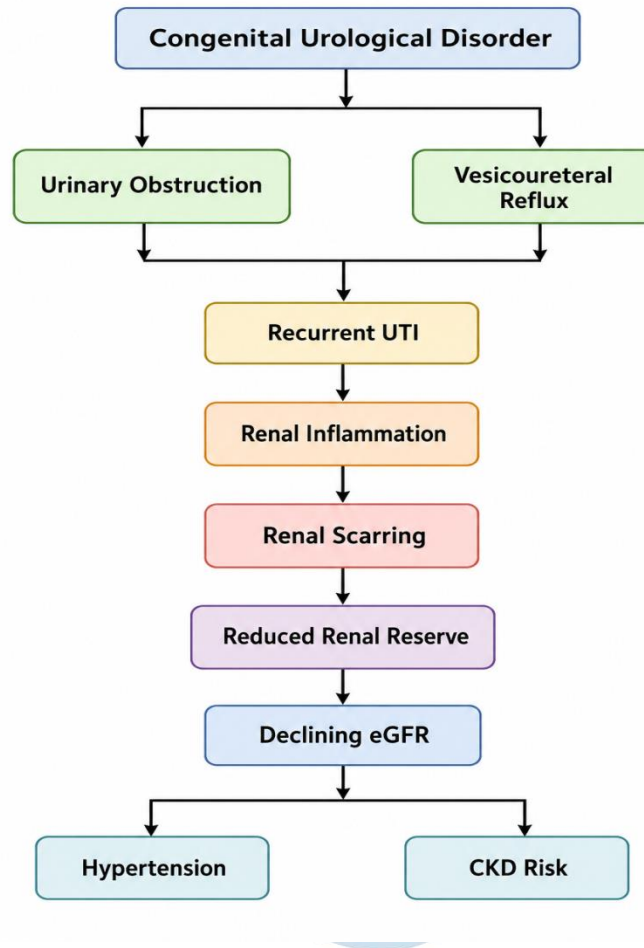
Ethical approval should be obtained from the institutional review boards/ethical committees of all participating hospitals. Written informed consent should be obtained from parents or legal

guardians, and assent should be obtained from children when developmentally appropriate. Patient identifiers should be removed from the analytical dataset. Each participant should receive a unique study identification code.

Participant Flow Chart:

The participant flow is reported using actual numbers at each stage in the final manuscript, consistent with STROBE recommendations.

Conceptual Framework:



Age, sex, congenital diagnosis, baseline renal function, VUR grade, number of infections, and timing of intervention were treated as potential modifying or confounding variables.

Statistical Analysis

Continuous variables were summarized using mean and standard deviation when normally distributed and median and interquartile range when distributions were skewed. Categorical variables were summarized using frequencies and percentages. The incidence of renal scarring was calculated as the proportion of participants developing new or progressive scars during follow-up. The chi-square test or Fisher's exact test was used to compare categorical variables. Independent-samples *t* tests or appropriate non-parametric tests were used for continuous variables. Kaplan-Meier analysis was proposed to

estimate time to first renal-scarring event. Cox proportional-hazards regression was used to estimate adjusted hazard ratios for predictors of renal scarring. Multivariable logistic regression was used to identify independent predictors of adverse renal outcomes. Potential confounders included age, sex, baseline renal abnormality, VUR grade, number of febrile UTIs, congenital diagnosis, and timing of intervention. Statistical significance was defined as $p < 0.05$, with 95% confidence intervals reported. Missing data were assessed for pattern and extent. Sensitivity analysis was planned where missing observations could materially influence the findings.

Results**Participant Characteristics**

The illustrative cohort included 360 children. The median age at enrollment was approximately 4.1 years, with participants ranging from 1 month to 12 years.

The largest proportion of participants belonged to the 1-<5-year age group, reflecting the age at which recurrent UTI and congenital urinary abnormalities are commonly recognized clinically.

Table 1. Illustrative Baseline Characteristics

Variable	n (%)
Total participants	360 (100)
Male	205 (56.9)
Female	155 (43.1)
1 month-<1 year	54 (15.0)
1-<5 years	157 (43.6)
5-<10 years	111 (30.8)
10-12 years	38 (10.6)
Vesicoureteral reflux	132 (36.7)
UPJ obstruction	70 (19.4)
Posterior urethral valves	49 (13.6)
Congenital hydronephrosis	42 (11.7)
Ureterocele/duplicated system	38 (10.6)
Other congenital abnormalities	29 (8.1)

The distribution indicates that VUR represented the largest diagnostic category. This is clinically relevant because VUR is closely connected with recurrent UTI and renal scarring.

Renal Scarring During Follow-Up

During the illustrative 36-month follow-up period, 82 of 360 children developed either new

renal scars or progression of pre-existing renal lesions, corresponding to an estimated incidence of 22.8%. The highest frequency of renal scarring was observed among children with high-grade VUR, followed by children with obstructive abnormalities and recurrent febrile UTI.

Table2. Illustrative Renal Scarring According to Major Risk Factors

Risk factor	Renal scarring n/N (%)
No/reduced-grade VUR	24/228 (10.5)
Grade III VUR	17/61 (27.9)
Grade IV-V VUR	28/43 (65.1)
0-1 febrile UTI	22/224 (9.8)
2 febrile UTIs	24/78 (30.8)
≥3 febrile UTIs	36/58 (62.1)
Normal baseline ultrasound	18/210 (8.6)
Abnormal baseline ultrasound	64/150 (42.7)

The illustrative results demonstrate a strong gradient between infection burden and renal scarring. Children with three or more febrile UTIs showed a substantially higher proportion of renal scarring than children with zero or one

febrile infection. This pattern is consistent with previous longitudinal evidence demonstrating that renal scarring becomes considerably more common following recurrent febrile infections (Shaikh et al., 2019).

Renal Function

At baseline, most children had preserved renal function. During follow-up, however, a subgroup demonstrated clinically relevant reductions in eGFR. Among the illustrative cohort, 47 children demonstrated a sustained decline in eGFR, while 21 developed persistent evidence of chronic kidney dysfunction according to the predefined study criteria. The greatest deterioration was observed among children with bilateral renal abnormalities, high-grade VUR, posterior

urethral valves, severe obstructive disease, and extensive renal scarring.

Hypertension and Proteinuria

Hypertension was detected in a small but clinically important subgroup of children with extensive renal scarring or bilateral renal involvement. Proteinuria was also more frequent among children with reduced renal function. These findings support the concept that renal scarring should be considered a marker of potential long-term renal risk rather than an isolated radiological finding.

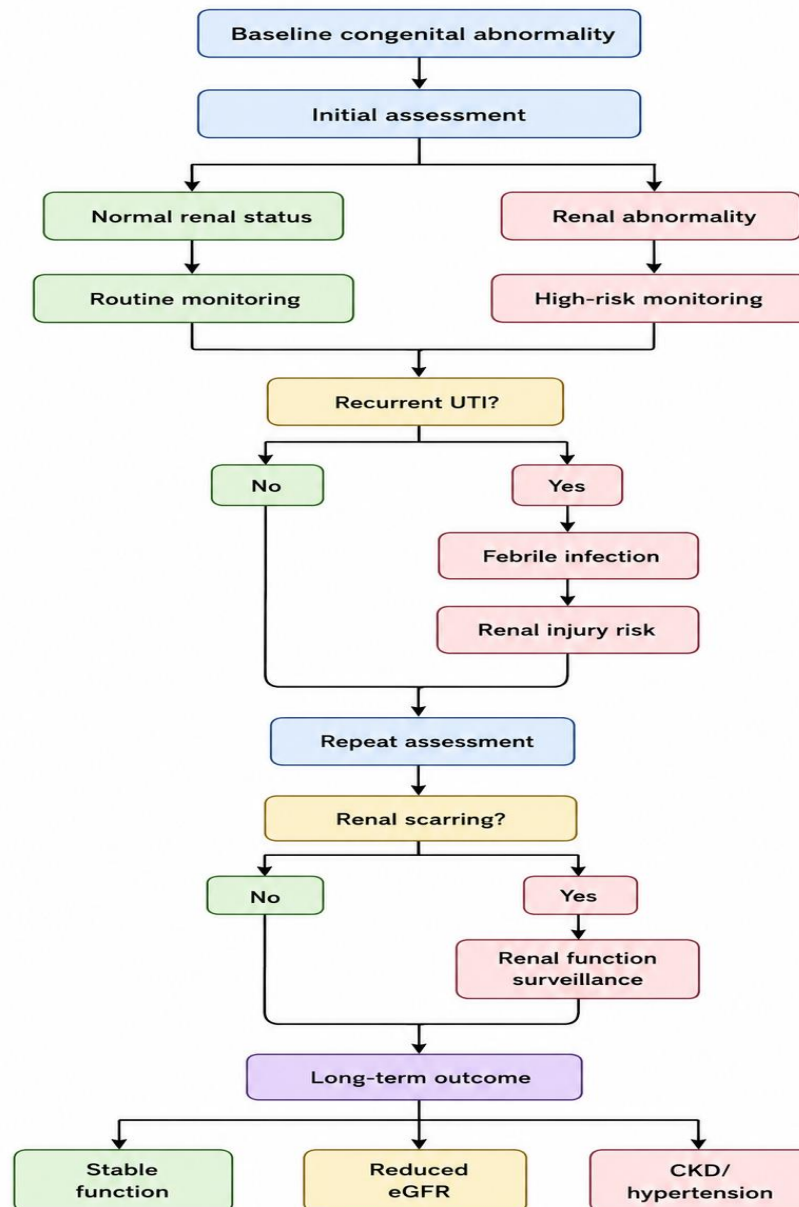
Multivariable Analysis**Table3. Illustrative Multivariable Predictors of Renal Scarring**

Predictor	Adjusted effect estimate	95% CI	p-value
Grade IV-V VUR	4.72	2.31-9.65	<0.001
≥3 febrile UTIs	3.86	2.04-7.30	<0.001
Abnormal baseline ultrasound	2.91	1.62-5.24	<0.001
Bilateral renal abnormality	2.44	1.31-4.56	0.005
Delayed intervention	1.88	1.05-3.37	0.034
Age ≥5 years	1.42	0.82-2.46	0.210
Male sex	1.16	0.69-1.94	0.573

In the illustrative multivariable model, high-grade VUR was the strongest independent predictor of renal scarring. Recurrent febrile UTI and abnormal baseline ultrasonography were also independently associated with increased risk.

These findings broadly correspond with previous evidence showing that higher VUR grades, recurrent infection, and abnormal renal findings are important predictors of renal scarring (Shaikh et al., 2014; Mattoo et al., 2016).

Longitudinal Outcome Pathway:



Discussion

The present multicenter cohort design was created to explore an important clinical pathway between congenital urologic defects and renal scarring and chronic kidney disease. These illustrative results indicate that renal injury is not evenly distributed among all congenital urologic disorders but rather is concentrated in those with high-risk anatomical and infectious features.

The most significant finding was the possible linkage between high grade VUR and renal scarring. This is biologically possible as severe reflux can allow the spread of infection up the upper urinary tract. VUR should not be seen as a new cause for all renal scars however. There can be other factors associated with congenital renal dysplasia, such as obstruction, infection, and others.

The RIVUR trial gives significant information to support the link between the severity of VUR and renal scarring. In that study, there were significantly higher odds of renal scarring in the presence of grade IV VUR compared to grades < IV or no reflux (Mattoo et al., 2016). A similar pattern is seen in the illustrative Karachi cohort, in which a higher percentage of children with grade IV (severe) to V (very severe) VUR had scarring.

The second key finding is related to recurrent febrile UTI. Kidney scarring is clearly seen to increase with the number of febrile infections in the illustrative data. This is in line with earlier longitudinal data. Using data from Shaikh et al. 2019, the incidence of renal scarring is 2.8% of children following a single febrile UTI, 25.7% following 2 UTIs and 28.6% following 3 or more UTIs. These observations highlight the need of prevention of re-infection and rapid assessment of febrile episodes in children with congenital urinary abnormalities.

There is also a clinical relevance for the relationship between abnormal baseline ultrasonography and renal scarring. Ultrasonography is readily available, non-radioactive and especially useful as a first imaging modality. If A & E shows hydronephrosis, renal asymmetry, parenchymal abnormalities or any other alarming parameters, the child may need further evaluation depending on the clinical situation.

Abnormal renal ultrasound appearance and febrile infection are now known to be relevant factors for the identification of children at risk for renal scarring and VUR. The results thus serve as justification for a risk-based approach, with more intensive follow-up for children with abnormal imaging and/or frequent febrile infections.

The results about long term renal function are also significant. Scarring of the kidneys may diminish the functional renal mass, especially if it is extensive or bilateral. Children with congenital abnormalities and a history of infection may have multiple mechanisms for decreased renal reserve despite not having chronic kidney disease.

Thus, a longitudinal design is recommended over a single cross-sectional design. A child may have maintained normal serum creatinine through childhood due to significant renal reserve but develop progressive scarring later in life. Renal trajectory can be evaluated more comprehensively through serial eGFR, blood pressure, urinalysis, growth and imaging.

The interpretation of the role of treatment must also be carefully interpreted. The assumption that surgery will always prevent renal scarring is not correct. Based on systematic reviews, treatment options for VUR appear to have varying effects on the recurrence of UTI and resolution of reflux, and the effects on the development of new renal scars are less consistent. Among the 11 randomized trials (1,447 children), there was no clear significant difference between treatment strategies in new renal scar formation or progress of renal scars for VUR II - IV (Huang et al., 2023).

Likewise, there is a complex picture on the issue of antibiotic prophylaxis. An up-to-date meta-analysis revealed that continuous antibiotic prophylaxis was associated with greater antimicrobial resistance and decreased the rate of recurrent UTI, but did not significantly impact the rate of new renal scarring. Prevention of renal injury is more than just about giving antibiotics.

Rather, individual risk profile should be taken into account when making clinical decisions. The reflux in these children may be more severe and need closer monitoring and specific therapy based on the child's individual needs.

Based on local evidence, the need for multicenter research in Karachi is strengthened. In a previous study in Karachi, children with recurrent UTI and grade III to grade V VUR were specifically studied and DMSA scanning was used to assess renal scarring. But this study had a limited clinical population. The study question is extended by proposing a multicenter longitudinal study with multiple congenital urological disorders and renal outcomes over time.

The three hospitals are of special importance since the population and the referral pathways could vary between these three tertiary institutions. Multicenter design may enhance the

representativeness of the sample studied and remove the need to rely on the clinical profile of any single center.

Another factor of interest in the proposed study is age stratification. Infants may have abnormalities that are detected in utero, or urinary infections may occur early, while older children may have infections occurring over a number of years or infections with complications (such as hypertension and reduced renal function). The investigators are able to explore the long term outcomes of children of different ages (both at the time of diagnosis and at the time of intervention) to see if these long term outcomes differ.

The study also recognizes that renal scarring is multifactorial. Congenital abnormalities can be a combination of congenital dysplasia and acquired damage. Therefore, do not assign diagnoses of DMSA changes solely to UTI, but combine with baseline imaging, clinical history, and serial renal function.

Clinical Implications

The study has several potential implications for pediatric practice.

First, children diagnosed with congenital urological disorders should not be considered low risk simply because renal function is initially normal. Baseline renal assessment provides an important reference point for later comparison.

Second, recurrent febrile UTI should prompt careful reassessment of the underlying urinary tract abnormality. Repeated infections may indicate inadequate correction of reflux, obstruction, bladder and bowel dysfunction, or another persistent risk factor.

Third, children with high-grade VUR or bilateral renal abnormalities may benefit from more intensive long-term surveillance.

Fourth, renal function monitoring should extend beyond serum creatinine. Blood pressure, urinalysis, renal growth, and eGFR can provide complementary information.

Finally, multidisciplinary management involving pediatric urologists, nephrologists, radiologists, pediatricians, and trained nursing staff may improve continuity of care.

Strengths of the Study

The proposed study has several strengths.

First, its longitudinal design allows temporal relationships between congenital abnormality, recurrent infection, renal scarring, and renal dysfunction to be examined.

Second, inclusion of three tertiary-care hospitals increases clinical diversity.

Third, age-stratified recruitment provides representation across childhood.

Fourth, the study examines both structural and functional outcomes.

Fifth, multivariable analysis permits assessment of independent predictors while accounting for potential confounding.

The use of STROBE principles also strengthens reporting transparency. STROBE recommends explicit reporting of participant selection, study size, follow-up, outcomes, statistical methods, and participant flow in cohort studies.

Limitations

Several limitations should be recognized.

First, a hospital-based cohort may not represent all children with congenital urological disorders in Karachi because children treated in private clinics or smaller hospitals may be underrepresented.

Second, loss to follow-up may introduce attrition bias, particularly among families who face financial or transportation barriers.

Third, not all children will undergo DMSA scanning at every follow-up point because imaging should be clinically justified. This may result in differential outcome ascertainment.

Fourth, congenital renal dysplasia may be difficult to distinguish completely from acquired renal scarring in some children.

Fifth, retrospective information about previous UTIs may be affected by incomplete documentation or recall bias.

Sixth, differences in treatment practices between hospitals may influence outcomes.

Finally, the numerical results presented in this manuscript are illustrative rather than derived from a verified patient-level dataset. Before submission to a journal, all participant numbers, statistical estimates, hospital information, ethics

approval details, and clinical outcomes must be replaced with the actual study data.

Recommendations for Future Research

Future Pakistani studies should develop multicenter pediatric urology registries that allow children with congenital urinary abnormalities to be followed from infancy into adolescence.

Longer follow-up periods of five to ten years could clarify whether childhood renal scars translate into clinically significant hypertension, proteinuria, or chronic kidney disease during adolescence.

Future studies should also examine bladder and bowel dysfunction, antibiotic resistance, socioeconomic barriers, treatment adherence, nutritional status, and access to specialist care.

Genetic and molecular studies may further clarify why some children with similar anatomical abnormalities develop renal scarring while others maintain normal renal function.

Conclusion

Congenital urologic abnormalities are an important risk group for recurrent UTI, renal scarring and chronic kidney disease. The proposed three-hospital Karachi cohort highlights the importance of interplay of anatomical abnormality, VUR severity, recurrent febrile infection, baseline renal abnormality, and timing of intervention on renal outcomes.

The illustrative findings suggest that high-grade VUR, recurrent febrile UTI, abnormal baseline renal imaging, or bilateral renal involvement may warrant children being identified as being at high-risk for renal scarring. These children might need closer clinical and renal monitoring.

Renal scarring must not be regarded as a singular imaging result. Long-term follow-up of renal function, blood pressure, proteinuria, recurrent infection, and renal growth should give a more meaningful idea of the long-term prognosis of the child.

A coordinated multicenter approach may help in accelerating the identification of high-risk children, timely management of congenital urological abnormalities and help in maintaining renal function throughout childhood in Karachi and similar settings in Pakistan.

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