

# Recurrent Urinary Tract Infections Risk Factors in Patients with Primary Vesicoureteral Reflux

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## ABSTRACT

**Background:** Knowing the risk of recurrence of urinary tract infection (UTI) in vesicoureteral reflux (VUR) can assist clinicians to sort therapeutic decisions. The current study's aim was to assess the association of UTI in VUR. Additionally, UTI recurrence might be predicted by the risk score.

**Materials and Methods:** This case-control study was carried out on 123 children at department of Paediatric, Saidu Group of Teaching Hospitals, Swat for the duration of one year from 1<sup>st</sup> July 2020 to 30<sup>th</sup> June 2021. Out of 123 children, the group-I had 57 children with documented previous UTIs history while group-II had 66 children with no previous UTIs and was referred to as a control group. All the patients were VUR diagnosed and were thoroughly followed up at a Renal Unit of single tertiary. UTI recurrence was referred to more than one follow-up episode. A regression model was used for independent variables identification regarding UTI recurrence. A questionnaire on bowel habits was provided to the parents. The abdominal plain film was evaluated by the observer and recorded on the documented scoring system. The constipation history was compared with the radiological and symptomatic scores. Organism single species with > 105/ml count in a single midstream catch of urine sample was reflected as UTI evidence.

**Result:** Out of 123 children, 88 (71.5%) were females while 35 (28.5%) were male. A total of 123 children had been investigated for UTI complaints. After the multivariable analysis adjustment, five recurrent UTIs predictor variables were the clinical presentation of UTI, female gender, reflux several grades, age less than 6 months, and syndrome dysfunction elimination. The UTIs recurrence risk factors were classified as high, medium, and low with prevalence 52 (42%), 41 (34%), and 30 (24%) respectively. The prevalence of UTIs rate per person-month was 10.9 (95% CI, 9.8, 12.7), 8.2 (95% CI, 6.7, 9.1) for medium, and 5.2 (95% CI, 3.3, 5.5) for the low-risk group.

**Conclusion:** The formulation of therapeutic strategies can be done based on prediction model for UTIs recurrence besides early detection of morbidity long-term risk for the patients.

**Keywords:** Vesicoureteral reflux, Urinary tract infection, Dysfunctional voiding, Constipation

## INTRODUCTION

Hypertension, renal scarring, and later-stage renal disease of children are prompts by the primary vesicoureteral reflux (VUR) and urinary tract infection (UTI) combination [1-3]. Subsequently, renal failure or injuries prevention of children from VUR further infection could be managed by current strategy and treatment [4]. Surgical correction and long-term prophylaxis (antimicrobial) have been the two main motilities for treatment. VUUR's natural tendency to improve medical management and time is relatively covered by the renal damage duration caused by VUR [5]. The risk of UTI recurrence in individual children should be considered by clinicians with established medical management. Vesicoureteral reflux (VUR) chances increased in children of age below 5 years. VUR chances increased with associated constipation. Bowel habits should be inquired for UTIs infection evaluation. Constipation relief can result in disappear UTIs recurrence [6]. Hypertension risk and renal failure increased as renal scarring comes from severe bilateral caused by subclinical infection of UTIs long-term consequences. Therefore, serious consideration must be taken even for a single UTI. Asymptomatic bacteria is clinically silent among some children. Spontaneous remission might appear in children within few months and better to be left untreated. Asymptomatic bacterial reflux was found in 11% cases [7].

The proportion of VUR and renal scarring was found 35% and 10-25% cases upon screening of asymptomatic school-aged children. Undiagnosed infection and UTIs symptomatic prior history were found among many of these children [8]. The distinction between subclinical infection and asymptomatic was difficult to be found in the laboratory or clinically.

Constipation is undiagnosed and poorly treated pediatric problem. People especially children's guardians should be aware of constipation complications and effects. Larger fecal reservoirs have been recorded in rectal manometry and examination in children of repeated UTIs. As the micturition increases among children, renal tract dilatation and residue bladder significantly increased constipation and improved with treatment [9]. Urinary tract infection and vesicoureteral reflux caused by detrusor stretch receptors simulation by inhibited bladder and emptying loaded impair rectum bladder due to mechanical load in chronic constipation [10]. Number of researchers described the correlation between UTIs and severe constipation among children and found that loaded rectum due to mechanical effect and sigmoid colon distortion leads to urethra elongation and bladder displacement thus causing emptying impaired bladder and hydronephrosis [11]. One study showed emptying impaired bladder association with constipation [12]. Another study reported a

large rectal reservoir found by manometry and rectal examination of UTIs history in children prior to constipation [13]. The present study was carried out to analyze outcome and adolescents of children with primary VUR with aims to find the UTIs recurrence rate and risk factors for medical treatment.

**MATERIALS AND METHODS**

This case-control study was carried out on 123 children at department of Paediatric, Saidu Group of Teaching Hospitals, Swat for the duration of one year from 1<sup>st</sup> July 2020 to 30<sup>th</sup> June 2021. Out of 123 children, the group-I had 57 children with documented previous UTIs history while group-II had 66 children with no previous UTIs and was referred to as a control group. All the patients were VUR diagnosed and were thoroughly followed up at a Renal Unit of single tertiary. UTI recurrence was referred to more than one follow-up episode. A regression model was used for independent variables identification regarding UTI recurrence. A questionnaire on bowel habits was provided to the parents. The abdominal plain film was evaluated by the observer and recorded on the documented scoring system. The constipation history was compared with the radiological and symptomatic scores. Organism single species with > 105/ml count in a single midstream catch of urine sample was reflected as UTI evidence. All the patients with primary VUR followed by three months duration were included in this study. Patients with neurogenic bladder, ectopic ureterocele, obstructive uropathies, and posterior urethral valves were excluded.

Conventional voiding cystourethrography was used for VUR diagnosis at the time of admission. A systematically proposed reflux grade was categorized as first voiding cystourethrography. A single dose routine of 1 to 2 mg/kg nitrofurantoin and trimethoprim was followed to maintain antibiotic prophylaxis among children. VUR correction was done with antibiotics prophylaxis failure as indicated surgical procedure for severe reflux. A systematic protocol was followed after the initial investigation. Our study prime outcomes were incidence of UTI and infections through recurrent UTI break through. The predictive variables for our study were gender, age, lower UTI, dysfunctionality syndrome (lower UTIs and constipation), renal damage, VUR grade (mild/moderate/severe), clinical presentation (fetal hydronephrosis/UTI), reflux laterality (unilateral/bilateral) and renal damage severity.

**RESULTS**

A total of 123 children had been investigated for UTI complaints. Out of 123 children, 88 (71.5%) were females while 35 (28.5%) were male. After the multivariable analysis adjustment, five recurrent UTIs predictor variables were the clinical presentation of UTI, female gender, reflux several grades, age less than 6 months, and syndrome dysfunction elimination. The UTIs recurrence risk factors were classified as high, medium, and low with prevalence 52 (42%), 41 (34%), and 30 (24%) respectively. The prevalence of UTIs rate per person-month was 10.9 (95% CI, 9.8, 12.7), 8.2 (95% CI, 6.7, 9.1) for medium, and 5.2 (95% CI, 3.3, 5.5) for the low-risk group. Of the total 123 patients, 88 (71.5%) were females and 35 (28.5%) were male as shown in Table/Figure-1. Table-2 demonstrates the

baseline characteristics such as age, the clinical presentation of 123 patients. Figure-2 shows the clinical presentation of 123 patients. The grade I-II reflux was 42 (34.1%), grade-III was 40 (32.5%) and Grade IV-V was 41 (33.3%). These grades of reflux such as I-II, III, and IV-V with their prevalence are shown in Table/Figure-3.

Table-1. Gender distribution of 123 Patients

Gender	Frequency (n)	Percentage (%)
Male	35	28.5
Females	88	71.5
Total	123	100

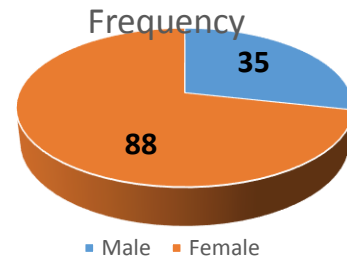


Figure-1 Gender distribution

Table-2. Baseline characteristics of 123 patients

Parameters	Value N (%)
Diagnosis Age (Months)	
Median	22.7
Interquartile range	9.9–43.5
Mean	31.3
SD	11.4
Clinical presentation	
Urinary infection	110 (89.5)
Fetal hydronephrosis	11 (8.9)
Familial history	2 (1.6)

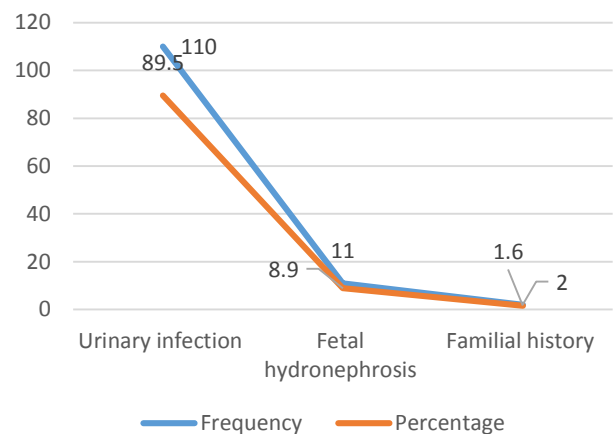


Figure-2. Clinical presentations of 123 patients

Table-3. Reflux grades for 123 patients

Grade of Reflux	Frequency (n)	Percentage (%)
I-II	42	34.2
III	40	32.5%
IV-V	41	33.3
Total	123	100

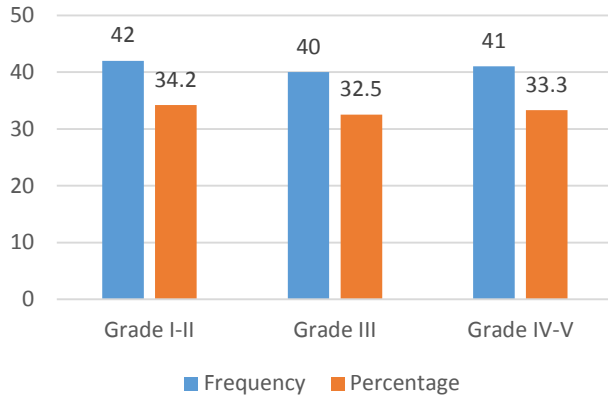


Figure-3: Grades of Reflux among 123 patients

Higher incidence of UTIs was significantly associated with variables such as female gender, age, DES, constipation. While VUR severe reflux grade (IV-V) was associated with UTIs higher incidence rate as shown in Table-4. Multivariable analysis involves nine different variables gender, LUTD, DES, clinical presentation, age, reflux grade, renal damage, and reflux laterality. Out of these five independent predictors for UTI recurrence were age, DES, female gender, severe grade, and clinical presentation as shown in Table 4.

Table-4 the incidence rate of UTIs with baseline characteristics.

Features	Incidence rate of UTIs	Ratio (CI, 95%)	P-value
Presentation		1.35(0.89, 2.0)	0.12
Fetal/other	(23/123)	6.4 (3.9, 9.2)	
UTI	(68/123)	8.5 (7.7, 9.5)	
Lower urinary tract dysfunction		1.6 (1.3, 2.0)	<0.001
Present	34/123	12.6 (10.6-15)	
Absent	89/123	7.3(6.5-8.2)	
Constipation		1.5 (1.2-1.7)	<0.001
Present	47/123		
Absent	78/123		
Dysfunctional elimination syndrome		1.5 (1.2-1.7)	<0.001
Present	53/123		
Absent	70/123		
Age <6 mo		1.48(1.2-1.7)	<0.001
Present	31/123		
Absent	93/123		

**DISCUSSION**

The current study investigated the UTI recurrence incidence with primary VUR and possible predictive variables in the pediatric population. Our investigation findings reported the UTI incidence rate decrease after reflux treatment at 24 months sharp changes. Five significant contributors were identified as risk factors associated with the UTIs recurrence frequency using multivariable analysis. Effective stratification of pediatric VUR was classified as low, medium, and high risks after medical treatment. The prevalence of UTI recurrence is higher among children despite careful follow-up and early management. In our study, about 37.5% of patients had UTI but uncommon recurrence. More than one episode of follow-up was presented among 16% of children. All these findings matched interestingly with another study [14-16]. In multivariable analysis, recurrent UTIs had five major predictive factors such as age, female gender, clinical presentation, DES, and reflux severity. Our study findings matched another study [17] conducted on 290 children with age <5years, symptomatic UTI (27%), recurrent UTI risk factors at age<6 months baseline and VUR grade. Gender distribution in our study was found insignificant but female’s prevalence was higher among 123 children in our study. Another study found 36% UTI recurrence among 226 children, without any difference between patients. The presence and absence of renal scarring were associated

with reflux grade. However, severe grades of reflux between III-V were stratified with no significant differences. Dysfunction elimination of the patients was 12 versus 7.6 per 1000 months in asymptomatic children [18-19]. Children with DES had a double risk for UTI recurrence compared to those without dysfunctional voiding and constipation [20].

Another study found primary VUR among 143 patients, out of which 70 children were breakthrough UTI, DES with 54(77%) [21]. One study reported severe reflux in infants showed 47% of children breakthrough but reached 69% of bladder dysfunction [22]. Another recent study showed VUR successful treatment with hyaluronic acids 2 months predictive factors including febrile higher risk and dysfunctional elimination [23]. VUR of effective children were stratified at three different degrees of UTI recurrence risk factors. A simple method of easily collected routine variables for clinical evaluation and imaging testing. Further studies need to be carried out for validating large and prospective series. The UTI recurrence incidence was decreased with intervention amenable factors in clinical implication of our analysis. Reflux severity, gender, and patients inherited conditions for recurrent UTIs were the most associated factors in our study. For managing UTIs, a target candidate remains only DES. UTI recurrence can be reduced by constipation and bladder dysfunction management. Comprehensive ultrasonography and clinical history details of the UTIs were mostly identified as DES.

Still, for infants, optimum management identification is troublesome [24].

## CONCLUSION

The formulation of therapeutic strategies can be done based on prediction model for UTIs recurrence besides early detection of morbidity long-term risk for the patients.

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