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OUTCOME OF VESICOUERTERAL REFLUX IN CHILDREN AT KING ABDULAZIZ UNIVERSITY HOSPITAL: RETROSPECTIVE STUDY

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Background:
Vesicoureteral reflux (VUR) classified as a congenital anomaly of the kidney and urinary tract and the most frequent among the pediatric population .VUR is the backflow of the urine from the bladder up into the ureter and the kidney .The complication of the disease could result in recurrent urinary tract infections (UTI) , hypertension, and renal scarring. Which may further progress, ending up with permanent kidney damage The aim of this study is to further explore the natural history of the disease, management, and the long-term sequelae of VUR in the pediatric population in King Abdulaziz University Hospital, Jeddah.
Methods: *Retrospective cohort study, this study was approved by the research ethics committee of King Abdulaziz University hospital from January 2010 to July 2017.A retrospective review was conducted on the records of pediatric patients diagnosed with Vesicoureteral reflux (VUR) either primary and secondary ages 0-18.*
The diagnosis of VUR was based upon the demonstration of reflux of urine from the bladder into the upper urinary tract by contrast voiding cystourethrogram (VCUG).
Results: *Among the103 patients assessed, 74 (71.8%) were males, The mean age at the time of diagnosis was 2.2 (± 3.1) years, and 63 (63.6%) were diagnosed at the first year of their life . There were no significant associations in the distribution of VUR outcomes by gender or age at diagnosis . The grades of VUR before and after surgery, where grade 5 reduced significantly from 54.2% before surgery to only 12.2% after surgery, p-value < 0.05.*
Conclusion: *This study found that male patients have a higher prevalence of VUR than females.*
And most of the patients diagnosed at the first year of their life.
UTI is more frequent among patients with CKD and unresolved VUR. Furthermore, antireflux surgery resulted in decrease the severity of VUR

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INTRODUCTION:

Vesicoureteral reflux (VUR) classified as a congenital anomaly of the kidney and urinary tract and the most frequent among the pediatric population [1, 2].VUR is the backflow of the urine from the bladder up into the ureter and the kidney which can contribute to the nature of this phenomena [2]. It's related to multiple anomalies in the urinary tract particularly in the function of the ureter, dynamics of the bladder, as well as the patency of the uretro-vesical junction (UVJ) [2]. The disease is manifested in 5 different grades and so the outcome may vary [1]. The complication of the disease could result in recurrent urinary tract infections (UTI) 40% [1,3], hypertension, and renal scarring. Which may further progress, ending up with permanent kidney damage and impaired renal function. However, VUR could spontaneously resolve [4, 5, 6]. In our country there is no sufficient data have been reported in viewing the magnitude and factors affecting VUR outcome. The aim of this study is to further explore the natural history of the disease, management, and the long-term sequelae of VUR in the pediatric population in King Abdulaziz University Hospital, Jeddah.

MATERIALS AND METHODS:

Retrospective cohort study, this study was approved by the research ethics committee of King Abdulaziz University hospital from January 2010 to July 2017.A retrospective review was conducted on the records of pediatric patients diagnosed with Vesicoureteral reflux (VUR) either primary and secondary ages 0-18.

The diagnosis of VUR was based upon the demonstration of reflux of urine from the bladder into the upper urinary tract by contrast voiding cystourethrogram (VCUG). The grades of VUR were defined according to the International Reflux Study Group (IRSG) classification system. The severity of VUR is classified as mild (grade I- II), moderate (III) and severe grade (IV-V).

UTI diagnosis was based on positive urine culture with colony count of more than 100,000 colony forming units/mL of a single pathogen. Glomerular filtration rate (GFR) was estimated by the Schwartz formula and chronic kidney disease stages were defined according to the National Kidney Disease Outcome Quality Initiative guidelines. Chronic kidney disease was defined as GFR <60 mL/min/1.73 m^2. national kidney foundation. Blood pressure values and definitions were based on the Fourth Task Force Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescence. +percentile

Recurrent UTI from NICE

Data collected from patients records were age, gender, clinical features, laboratory investigations (urine cultures, serum creatinine and hemoglobin), imaging [ultrasound scan (USS), VCUG and dimercaptosuccinic acid radionuclide (DMSA) scan], past surgeries and medication, current treatment, and outcome measures (recovery, chronic kidney disease, hypertension, renal scar, and death).

Statistical analysis was performed using the SPSS software.

Statistical Analysis

Descriptive statistics were used to describe the characteristics of the study participants. Mean and standard deviations (SD) are reported for continuous variables. Frequencies with proportions were reported for categorical variables. Pearson chi-square test was used to compare outcomes by gender. Statistical significance was set at $p < 0.05$. Analysis was performed using Statistical Package for Social Science (SPSS), version 23 (IBM, Armonk, NY, USA).

RESULTS:

Among the103 patients assessed, 74 (71.8%) were males, with mean age of 7.8 (±5.0) years. The mean age at the time of diagnosis was 2.2 (± 3.1) years, and 63 (63.6%) were diagnosed at the first year of their life (Table 1). 40.8% of the total VUR cases were due to primary causes. The main clinical presentation was UTI in 73.8 % and recurrent UTI was found in 23.3 % (Table 1). There were no significant associations in the distribution of VUR outcomes by gender or age at diagnosis (Table 2 &3). Spontaneous resolution was found in 10.3 of female and 4.1 % in male%. Resolution after surgery was found in 27.6 of female and 25.7 in male (Table 2). Table 3 shows that 15.6% of VUR cases diagnosed after the first year of life were not resolved, 20.8% were resolved after surgery, and 10.4% turned into a chronic kidney disease (CKD). Table 4 demonstrates the grades of VUR before and after surgery, where grade 5 reduced significantly from 54.2% before surgery to only 12.2% after surgery, p-value < 0.05.

Primary vs secondary VUR outcome. By using the chi square it was found that there is a significant difference between the outcome of primary and secondary VUR (P = .003). The results show that 60.4% of the patients with primary VUR are improving with surgical intervention and about 33.3% of the patients with secondary VUR are improving with surgery.

Table 1 Characteristics of patients with VUR

Gender	
Male	74 (71.8)
Female	29 (28.2)
Age, years	
Mean (±SD)	7.8 (±5.0)
Age at diagnosis, years	
Mean (±SD)	2.2 (±3.1)
Nationality	
Saudi	66 (64.1)
Non-Saudi	37 (35.9)
Type of VUR	
Primary	42 (40.8)
Secondary	61 (59.2)
Age at diagnosis	
Antenatal	4 (4.0)
At birth	10 (10.1)
Within first month	17 (17.2)
>1-12 month	32 (32.3)
>12 month	36 (36.4)
Presenting symptom	
UTI	52 (50.5)
Recurrent infection	24 (23.3)
Antenatal	27 (26.2)

SD= standard deviation, VUR= vesicoureteral reflux, UTI = urinary tract infection

Table 2 Distribution of VUR outcomes by gender, n (%)

Outcome	Total	Female	Male
Spontaneous resolution	6 (7.7)	3 (10.3)	3 (4.1)
Not resolved	27 (34.6)	7 (24.1)	20 (27.0)
Resolved with surgery	27 (34.6)	8 (27.6)	19 (25.7)
Hypertension	2 (2.6)	0 (0)	2 (2.7)
Chronic Kidney Disease (CKD)	12 (15.4)	2 (6.9)	10 (13.5)
Other	4 (5.1)	1 (3.4)	3 (4.1)

P = > 0.681

Table 3 Distribution of VUR outcomes by age at diagnosis, n (%)

Outcome	Antenatal-1 month	>1-12month	>12 month
Spontaneous resolution	3 (3.9)	0 (0)	3 (3.9)
Not resolved	10 (13)	5 (6.5)	12 (15.6)
Resolved with surgery	7 (9.1)	3 (3.9)	16 (20.8)
Hypertension	2 (2.6)	0 (0)	0 (0)
CKD	2 (2.6)	2 (2.6)	8 (10.4)
Other	1 (1.3)	1 (1.3)	2 (2.6)

P= 0.533

Table 4 Grades of VUR before and after surgery

Grades of VUR	Before Surgery	After surgery
0		19 (25.7)
I	8 (8.3)	3 (4.1)
II	1 (1.0)	2 (2.7)
III	12 (12.5)	4 (5.4)
IV	23 (24.0)	3 (4.1)
V	52 (54.2)	9 (12.2)

P= < 0.05

Table shows the relationship between outcome of VUR and frequency of UTI

Outcome	Frequency of UTI/Year	
	2-3	> 3
Not Resolved	2 (18.2)	2 (18.2)
Resolved with surgery	1 (9.1)	1 (9.1)
Hypertension	0 (0)	1 (9.1)
CKD	3 (27.3)	1 (9.1)

UTI is more frequent among patients with CKD and unresolved VUR. Of the total of patients with recurrent UTI, 18% of them with unresolved VUR experience more than 3 times per year frequency of UTI.

Table.

Type of VUR	Antenatal Hydronephrosis		Total
	Yes	No	
Primary	11 (28.2%)	28 (71.8%)	39 (100%)
Secondary	20 (37%)	34 (63%)	54 (100%)

52 (50.5)
24 (23.3)
27 (26.2)

DISCUSSION:

Similar to other studies, the data showed male predominance, with male to-female ratio of 4:1. However, there is no association between the gender nor age at diagnosis in predicting the sequel of VUR. Which is consistent with previous literature showed that gender alone was a poor predictor of clinical outcome in patients diagnosed with primary VUR. [10] While other studies, showed that male gender alone is a significant risk factor for renal scarring. [13] This could be attributed to the relative small sample size in this study.

Patterns and frequency of presentation in patients with VUR is presented in table 1. Out of the 103 patients enrolled in this study, half of our population presented with urinary tract infection, and (%23.3) presented with recurrent infection while the remaining (%26.2)were antenatally detected with hydronephrosis .Similarly there was a study conducted in Saudi Arabia found most of cases and up-to 70% of their population presented with UTI (9).

Many children who presented with UTI had clinical signs and symptoms of infection. Of those presented with UTI, 26.9% were atypical. Non ecloi were found in (10) 71.42%, HTN (2) 14.3%, Renal failure (1) 7.14%, not responding to antibiotic in 24 hours (7.14%).

42 out of 103 patients (40.8%) were due to primary causes, while the other 61 patients (59.2%) were due to secondary causes including, PUV 26.2%, neurogenic bladder 47.5%, other obstructive uropathy 26.2%.

Secondary VUR was associated with significantly higher incidence of UTI , as 45.5% had UTI 2-3 times a year, compared to 9.1% of primary VUR in whom had UTI 2-3 attach/year. In contrast to another study which showed that children with primary VUR had a higher number of UTI was a significant risk factor for renal scarring (15).

Severity of VUR was correlated with the frequency of UTI in a proportional representation, the higher the grade of VUR the higher the frequency of UTI (p=0.05). On the other hand, the frequency of UTI is directly proportional to a worse VUR outcome (p=0.05).

Among patients with unresolved VUR (18%) experienced 3 times UTI infections more than resolved VUR patients. Which emphasize early diagnosis, monitoring, and management is essential to reach a better outcome in VUR patients.

15.6% of VUR cases diagnosed after the first year of life were not resolved, 20.8% were resolved after surgery, and 10.4% turned into a chronic kidney disease (CKD). With the possibility of such deliberating consequence, early identification of cases with asymptomatic VUR might be useful to prevent these dire consequences.

Those with milder grade VUR showed better response to surgical intervention than those with higher grades. (table 4).

Almost one third of our patients were asymptomatic and were discovered by MCUG finding after routine

investigations. A high index of suspicion is a key to an early diagnosis of VUR. It's worth to mention that even mild grade VUR have showed permanent renal scar and damage.

Surgery can drastically change or even reverse the grade of VUR. Moreover, grade V reduced significantly from 54.2% before surgery to 12.2% after the surgery (Table 4).

VUR in experimental and clinical trials has gained relevance in the last three decades. As a result, some progress has been made in the description of the natural history of the disease and the well-established tendency toward spontaneous resolution of the condition, as seen in 45.7%of the subjects in our series. In patients with prenatally diagnosed VUR, the trend toward spontaneous resolution is even stronger depending on the severity of the involvement. (16) our study showed a spontaneous resolution rate of 7.8%, however no spontaneous resolution was documented in those diagnosed between 1-12 month. Some limitations were noticed, like loss of continuity in the follow-up of some patients and the lack of complete data, to name a few, which considerably decreased the number of patients eligible for analysis.

CONCLUSION:

This study found that male patients have a higher prevalence of VUR than females.

And most of the patients diagnosed at the first year of their life.

The secondary VUR causes have a high predominance than the primary causes.

UTI is more frequent among patients with CKD and unresolved VUR. There were no significant associations in the distribution of VUR outcomes by gender or age at diagnosis. Furthermore, antireflux surgery resulted in decrease the severity of VUR.

Recommendation

2ndary cause worst outcome monitor, early surgical intervention.

Surgical intervention in higher grade.

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