

Voiding dysfunction in children causes, management, and prognosis

A single-center retrospective study

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ABSTRACT

الأهداف: نستعرض 3 أسباب مختلفة لإعتلال التبول؛ متلازمة اعتلال التبول الوظيفي (DVS)، المثانة العصبية الناتجة عن الصلب المشقوق (NB) ومتلازمة المثانة والصمام (VBS).

المنهجية: أجرينا دراسة متابعة استيعادية من مركز واحد حول الأطفال الذين يعانون من إعتلال التبول في مستشفى جامعة الملك عبد العزيز، جدة، المملكة العربية السعودية خلال الفترة من 2005م إلى 2017م.

النتائج: اشتملت الدراسة على مائة وتسعة وتسعون طفلاً (67.3% صبياً)، 75 مريض مصاب بمتلازمة اعتلال التبول الوظيفي (DVS) في المجموعة الأولى، و64 مريض بالمثانة العصبية الناتجة عن الصلب المشقوق (NB) في المجموعة الثانية، و60 مريض يعاني من متلازمة المثانة والصمام (VBS) في المجموعة الثالثة. قمنا كذلك بتصنيف وفقاً للغة العمرية وقت بداية العلاج؛ الرضع (46%)، الأطفال الصغار (27%) والذين تتراوح أعمارهم في سن المدرسة (28%). وبالنسبة لفئات العلاج؛ 31% احتاجوا إلى الملاحظة فقط، و25% احتاجوا إلى القسطرة التنظيفية المتكررة CIC، و13% احتاجوا إلى جراحة فقط، و31% احتاجوا إلى كل من الجراحة مع القسطرة التنظيفية المتكررة. واشتملت الاعتلالات المصاحبة؛ على اتساع حوض الكلى (81%)، وارتجاع البول الثانوي (47%) (VUR)، والتهابات حوض الكلى (37%) والندب الكلوي (60%)، وكلها لها تأثير سلبي على معدل فلترة الكلى (eGFR). كشفت دراسات تخطيط ديناميكية المثانة عن ضعف امتثال المثانة في (57.6%) والمثانة المرتمخية في (1.1%). تطور المرض الكلوي المزمن في (22%)، وبدأنا العلاج بالبدائل الكلوية في 11.5% وتوفي 4% بسبب المرض الكلوي. وقد لاحظنا تحسناً عاماً في معدل فلترة الكلى eGFR عند انتهاء الدراسة في كل المجموعات الثلاث ($p < 0.001$)، ولكن مجموعة متلازمة المثانة والصمام VBS كانت الأقل تحسناً ($p = 0.021$). كان هناك ارتباط سلبي بين العمر عند بداية العلاج ومعدل فلترة الكلى eGFR عند انتهاء الدراسة ($p = 0.002$).

الخلاصة: يرتبط التشخيص والعلاج المبكر لإعتلال التبول لدى الأطفال بنتائج أفضل. الأطفال ذوو العلاج التحفظي أفضل حفاظاً على وظائف الكلى من أولئك الذين يحتاجون إلى عمليات جراحية.

Objectives: To review voiding dysfunction caused by 3 different etiologies; dysfunction voiding syndrome (DVS), neurogenic bladder secondary to spinal dysraphism (NB), and valve bladder syndrome (VBS).

Methods: A single-center retrospective study on children with voiding dysfunction followed up at King Abdulaziz University Hospital, Jeddah, Saudi Arabia from 2005 to 2017.

Results: One hundred and ninety-nine children (67.3% boys) were included: Group 1 (n=75, DVS), Group 2 (n=64, NB), and Group 3 (n=60, VBS). Further classification according to the age at presentation; infants (46%), toddlers (27%) and school aged (28%). Management categories: 31% children needed observation only, 25% needed clean intermittent catheterization (CIC), 13% needed only surgery and 31% needed both surgery and CIC. Associated comorbidities: hydronephrosis (81%), vesicoureteral reflux (47%), pyelonephritis (37%) and renal scar (60%), all have negative impact on estimated glomerular filtration rate (eGFR). Urodynamic studies revealed poor bladder compliance in 57.6% and atonic bladder in 1.1%, progression to chronic kidney disease (22%), commenced on renal replacement therapy 11.5% and 4% died with ESKD. Overall improvement in the last eGFR is observed ($p < 0.001$), but VBS group was the least to improve ($p = 0.021$). There was a negative correlation between the last eGFR and age at presentation ($p = 0.002$).

Conclusion: Early diagnosis and management of childhood voiding dysfunction was associated with better prognosis. Children managed conservatively have better preservation of kidney function than those who needed surgery.

Keywords: dysfunction voiding syndrome, Hinman's syndrome, neurogenic bladder, post valve bladder

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Normal bladder function involves storage of urine at low pressure and adequate filling volume followed by voiding with adequate detrusor contraction associated with relaxation of the sphincter that leads to near complete bladder emptying. Neuropathic or neurogenic bladder (NB) is considered an important risk factor for pyelonephritis and chronic kidney disease (CKD).¹ It is a variable entity that may result from a variety of conditions affecting the nervous systems.² Neuro-spinal dysraphism is the most common cause of childhood neuropathic bladder.³ Detrusor-sphincter-dyssynergia is a bladder contraction with concurrent involuntary contraction of the external urethral sphincter, and urodynamics study is required for diagnosis.⁴ Ongoing research to minimize the significant current impact of the pediatric neurogenic bladder by improving the understanding of optimal choice of candidates for each management strategy continuous to be needed.⁵ Hinman's syndrome or dysfunction voiding syndrome (DVS) is a rare disorder characterized by bladder dysfunction without spinal lesions. It may present in early infancy as well in preschool children with recurrent urinary tract infection (UTI), constipation, enuresis, and increased post-void residual urine volume.⁶ The International Children Continence Society (ICCS) refers dysfunctional voiding to neurologically normal individuals with an intermittent or fluctuating urinary flow caused by involuntary intermittent contraction of the striated muscle of the pelvic floor during voiding or the external urethral sphincter; it can be diagnosed with uroflowmetry.⁷ Children born with posterior urethral valves (PUV) often have bladder dysfunction characterized by over-activity or low compliance in infancy, but later in life, the bladder tends to empty poorly and becomes oversized.⁸ In this study, we have evaluated the prognosis of voiding dysfunction; and its associated morbidities and managements.

Methods. We have conducted a retrospective study of voiding dysfunction in children followed up at King Abdulaziz University Hospital, Jeddah, Saudi Arabia from 2005 to 2017. Children were classified into 3 groups according to the underlying etiology: Group 1 - DVS; Group 2 - NB secondary to a spinal dysraphism; and Group 3 - bladder dysfunction associated with PUV-valve bladder syndrome (VBS).

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Demographic data was collected including age at presentation, gender, and duration of follow-up, clinical data and CKD staging according to the estimated glomerular filtration rate (eGFR) using Schwartz formula.⁹

Further classification according to the age at presentation, infants (up to one year), toddlers (1-5 years), and school aged (5-16 years). Diagnosis of voiding dysfunction was made by clinical picture, voiding diary, radiological assessment, and urodynamic study. We documented the associated comorbidities such as pyelonephritis, proteinuria, hypertension, hematuria, and progression of CKD. All radiological findings were documented, including ultrasound of the kidney, ureter and bladder (KUB), micturating cystourethrogram (MCUG), di-mercapto-succinic acid (DMSA) scan, diuretic renogram: diethylenetriamine penta-acetic acid (DTPA)/technetium 99 mercapto-acetyl-triglycine scan (MAG3), and lower spinal magnetic resonance imaging (MRI), to identify spinal defects especially in DVS and NB groups. We reported the incidence of vesico-ureteral reflux (VUR), hydronephrosis, renal scarring, results of urodynamic studies, and the types of surgical intervention.

Our protocol of management of children with voiding dysfunction include; medical treatment with prophylactic antibiotics for recurrent pyelonephritis, timed voiding, double micturition, biofeedback training, oral anticholinergic medications for poor compliant bladder, beside management of constipation. Clean intermittent catheterization (CIC) 4-6 time/day is indicated for children with high leaking pressure >40cm H₂O or high residual urine volume. Vesicostomy is indicated in certain condition like inability to urinate, or poor compliance to CIC, especially in tiny babies with progressive loss of kidney function. A third classification of our cohort were made according to the category of management: category 1; included children who did not need CIC or surgery, category 2; children who needed CIC but did not need surgery, category 3; children who have surgery but they did not need CIC, category 4: children who needed both CIC and surgery. We reported the incidence of end stage kidney disease (ESKD), and the frequency of renal replacement therapy (RRT). Finally, the mortality due to CKD complication or ESKD was reported for each group.

We defined, proteinuria ≥ 300 mg/L, hematuria >10 high powered field (HPF), hypertension, >95th percentile for age, gender, and height, CKD progression; worsening of eGFR ≤ 60 ml/min/1.73m², ESKD; eGFR ≤ 15 ml/min/1.73 m². Botox involves injection of botulinum toxin (botox) into the bladder wall.

Mitrofanoff procedure involves appendicovesicostomy where appendix is used to create channel; the urinary bladder with outside the body. Monti procedure means ileo-vesicostomy, using part of the ileum to connect urinary bladder with outside the body.

Inclusion criteria included all children diagnosed with voiding dysfunction due to Hinman's syndrome, spinal dysraphism and post valve myogenic bladder dysfunction. The exclusion criteria was patients with neurogenic causes other than spinal dysraphism, patients who have PUV not associated with bladder dysfunction and patients with other congenital causes of bladder wall dysgenesis.

The Ethics Research Committee at the Faculty of Medicine, King Abdulaziz University (KAU) approved this study. Consent from the participants was waived, as we studied anonymous subjects retrospectively and did not include any specific interventions. The study is fulfilling the ethical principles of the Declaration of Helsinki.

Statistical analyses. The Statistical Package for Social Sciences (SPSS), version 23 (IBM Corp, Armonk, NY, USA) was used for analysis. Non-normally distributed data was presented in median and range. A p -value <0.05 is considered significant, and data was presented with the 95% confidence intervals (CIs). We used different non-parametric tests during the analysis for median comparison, Mann-Whitney U-test for dichotomous variables, Kruskal-Wallis for polychotomous variables, and Wilcoxon test for repeated eGFR (initial and last measurements) in a single group. The Chi-square test was used between-group comparisons of categorical variables. For correlation, we used Point biserial correlation (Spearman correlation). Microsoft PowerPoint 2019 was used to create the figures.

Results. In this study, 199 children were included in the study (134 boys, 67.3%). Group 1 (DVS): 75 children (44 boys, 58.6%), Group 2 (NB): 64 children (30 boys, 46.8%), and Group 3 (VBS): 60 boys.

Table 1 summarize patient's demographic data, age groups at presentation, different types and frequencies of surgical intervention and the different categories of management. Ninety-one (45.7%) children was diagnosed and started management in infancy, there was a significant improvement in the median eGFR ($p<0.001$, **Figure 1**), while no significant changes in the median eGFR have occurred in toddlers ($p=0.17$), and school aged ($p=0.14$) groups. Also, there was a significant negative correlation between age at presentation and the last follow up eGFR ($p=0.002$, **Figure 1**).

Table 2, presents the clinical data, associated morbidities, types of RRT, and mortalities. Hydronephrosis ($p=0.002$), hypertension ($p=0.013$), proteinuria ($p=0.007$), and hematuria ($p=0.012$) were significantly higher in DVS group compared to NB and VBS groups.

Overall significant improvement in the median of the last eGFR was observed among the 3 studied groups ($p<0.001$), although VBS group was the least to improve ($p=0.02$).

In the management categories: 62 (31%) children needed observation only, 50 (25%) children needed CIC, 25 (13%) children needed surgery without CIC, and 62 (31%) children needed both surgery and CIC. The effects on the median of the last follow up eGFR is displayed in **Figure 2**. Those who have normal bladder compliance and did not need either CIC or surgical intervention have the best preservation of kidney function. Furthermore, children required CIC without the need for surgery showed significant difference in eGFR compared with those who needed surgical intervention ($p=0.001$). Vesicostomy is the primary surgical management in 40 (20.1%) patients. Children who had vesicostomy showed significant lower median last eGFR than whom did not need vesicostomy ($p<0.001$, **Figure 3**).

Pressure monitored urodynamic evaluation was performed in 85 (42.7%) children. It revealed poor bladder compliance (namely, impaired bladder capacity) in 49 (57.6%), atonic bladder in one child (1.1%), and normal bladder compliance in 35 (41.1%) children, the remaining children either refused or were uncooperative during the procedure.

Unilateral or bilateral hydronephrosis was positive in 81%, and 47% have VUR. There was a significant difference in the median of the last eGFR ($p=0.003$) in comparison with the negative group ($p=0.001$, **Figure 3**). Renal scar was found in 62% of those who had DMSA scan. The difference in median eGFR with the negative group was borderline significant ($p=0.053$). Similarly, pyelonephritis in 102 (37%) children negatively affected the last eGFR ($p=0.045$) when compared with the negative patients (**Figure 3**).

Discussion. We have observed overall good preservation of kidney function among the 3 studied groups; however, a significant percentage still have progression to CKD (22%), 11.5% required renal replacement therapy, and 4% died with ESKD. This highlights the voiding dysfunction as an important cause of CKD in children. Dysfunction voiding syndrome (the

Table 1 - Baseline patients' demographic and disease characteristics (N=199).

Baseline demographics	Total	DVS (n=75)	NB (n=64)	VBS (n=60)
		n (%)		
Male	134 (67.3)	44 (58.6)	30 (46.8)	60 (100)
<i>Age at presentation (month)</i>				
Median (range)	24 (192)	48 (192)	24 (168)	9 (156)
Min (max)	0.024 (192)	0.024 (192)	0.024 (168)	0.024 (156)
Mean±SD	43.9±49.6	60.1±6.32	43.5±6.21	24.1±4.37
<i>Age at last follow-up (month)</i>				
Median (range)	108 (252)	120 (252)	120 (238)	88 (192)
Min (max)	12 (264)	12 (264)	14 (252)	12 (204)
Mean±SD	114.7±65.2	124.9±8.5	122.1±7.7	94.0±6.7
Follow-up duration by month median (range)	72 (180)	72.0 (156)	72.0 (180)	78.0 (144)
<i>Groups of age at presentation</i>				
Infancy up to 1 year	91 (45.7)	25 (33.3)	30 (46.9)	36 (60.0)
Toddler (1-5 years)	52 (26.1)	20 (26.7)	17 (26.6)	15 (25.0)
School age (5-16 years)	56 (28.1)	30 (40.0)	17 (26.6)	9 (15.0)
<i>Categories of management</i>				
Category 1	62 (31.2)	25 (33.3)	14 (21.9)	23 (38.3)
Category 2	50 (25.1)	15 (20.0)	19 (29.7)	16 (26.7)
Category 3	25 (12.6)	11 (14.7)	4 (6.3)	10 (16.7)
Category 4	62 (31.2)	24 (32.0)	27 (42.2)	11 (18.3)
<i>Surgical intervention</i>				
Negative	112 (56.3)	40 (53.3)	33 (51.6)	39 (65.0)
Positive	87 (43.7)	35 (46.7)	31 (48.4)	21 (35.0)
<i>Surgical intervention types</i>				
Vesicostomy	40 (20.1)	16 (21.3)	10 (15.6)	14 (23.3)
Iliocystoplasty	33 (16.5)	14 (18.7)	14 (21.9)	5 (8.3)
Ureterostomy	20 (10.0)	9 (12.0)	9 (14.1)	2 (3.3)
Botox	4 (2.0)	1 (1.3)	3 (4.7)	0 (0.0)
Mitrofanoff/monti	6 (3.0)	3 (4.0)	1 (1.6)	2 (3.3)

DVS: dysfunction voiding syndrome, NB: neurogenic bladder 2ry to spinal lesion, VBS: valve bladder syndrome, SD: standard deviation, Max: maximum, ESKD: end stage kidney disease, Botox: botulinum toxin injection into the bladder wall, Mitrofanoff: appendicovesicostomy, Monti: ileovesicostomy. Category 1: 62 children who did not need CIC or surgery, Category 2: 50 children who needed CIC but did not need surgery, Category 3: 25 children who have surgery but they did not need CIC. Category 4: 62 children who did need both CIC and surgery, CIC: clean intermittent catheterization

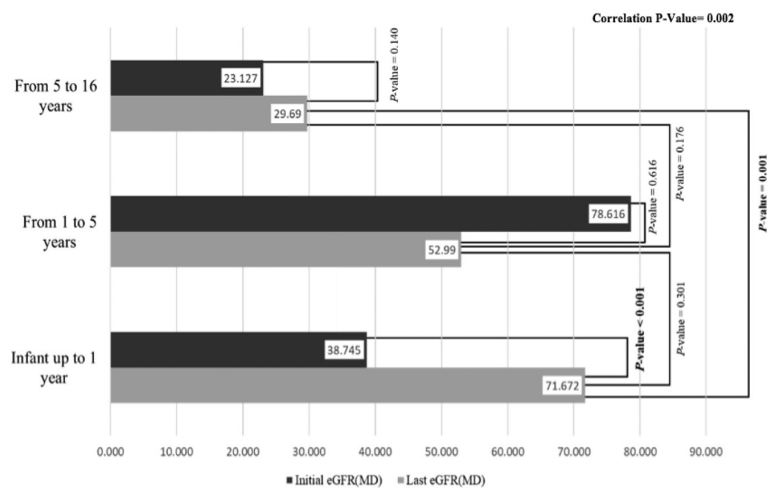


Figure 1 - Comparison between age at presentation and initial and last estimated glomerular filtration rate test.

Table 2 - Baseline clinical data of the 3 studied groups (N=199).

Baseline clinical data	Total	DVS (n=75)	NB (n=64)	VBS (n=60)	P-value
		n (%)			
Initial eGFR mL/min/1.73 m²					
Median (range)	39.61 (135.4)	45.15 (134.3)	66.2 (134.3)	23.1 (106.3)	0.001
Min (max)	3.2 (138.6)	3.6 (129.7)	4.3 (138.6)	3.2 (109.5)	
Mean±SD	50.1±2.77	49.8±36.9	66.2±44.04	33.1±27.9	
Last follow-up eGFR mL/min/1.73 m²					
Median (range)	59.97 (137.3)	55.0 (136.0)	90.8 (136.7)	37.7 (135.6)	0.000
Min (max)	3.1 (140.4)	4.2 (140.2)	3.7 (140.4)	3.1 (138.7)	
Mean±SD	66.4±3.3	65.1±46.1	84.9±46.1	48.2±40.6	
Comparison median initial eGFR: last eGFR, p-value	<0.001	<0.001	0.002	0.021	
Hydronephrosis					
Negative	38 (19.1)	8 (10.7)	21 (32.8)	9 (15.0)	0.002
Positive	161 (80.9)	67 (89.3)	43 (67.2)	51 (85)	
Unilateral	49 (30.4)	14 (20.9)	22 (51.2)	13 (25.5)	
Bilateral	112 (69.6)	53 (79.1)	21 (48.8)	38 (74.5)	
VUR					
Negative	105 (52.8)	34 (45.2)	46 (71.9)	25 (41.7)	0.618
Positive	94 (47.2)	41 (54.7)	18 (28.1)	35 (58.3)	
Unilateral	79 (84.0)	33 (80.5)	15 (83.3)	31 (88.6)	
Bilateral	15 (16.0)	8 (19.5)	3 (16.7)	4 (11.4)	
Scars on DMSA					
Negative	37 (38.1)	18 (47.4)	11 (28.9)	8 (38.1)	0.657
Positive	60 (61.9)	20 (52.6)	27 (71.1)	13 (61.9)	
Unilateral renal scars	34 (56.7)	10 (50.0)	17 (63.0)	7 (53.8)	
Bilateral renal scars	26 (43.3)	10 (50.0)	10 (37.0)	6 (46.2)	
Obstruction on DTPA/MAG3, n=144	65 (45.1)	20 (35.1)	22 (48.9)	23 (54.8)	0.125
CIC	113 (56.8)	40 (53.3)	46 (71.9)	27 (45.0)	
Oxybutynin	123 (61.8)	48 (64.0)	48 (75.0)	27 (45.0)	
Comorbidity					
Pyelonephritis	102 (37.2)	44 (58.7)	33 (51.6)	25 (41.7)	0.145
Hypertension	42 (15.3)	24 (32.0)	10 (15.6)	8 (13.3)	0.013
Proteinuria	24 (8.8)	13 (17.3)	1 (1.6)	10 (16.7)	0.007
Hematuria	5 (1.9)	5 (6.7)	0 (0)	0 (0)	0.012
Progressive CKD	61 (22.2)	22 (29.3)	17 (26.6)	22 (36.7)	0.452
End Stage CKD	40 (14.6)	14 (18.7)	9 (14.1)	17 (28.3)	0.132
RRT	23 (11.5)	11 (14.6)	4 (6.25)	8 (13.3)	
Non	176 (88.4)	64 (85.3)	61 (95.3)	52 (86.7)	
Hemodialysis	11 (5.5)	6 (8.0)	1 (1.6)	4 (6.7)	
Peritoneal	11 (5.5)	5 (6.7)	1 (1.6)	4 (6.7)	
Transplantation	1 (0.5)	0 (0.0)	1 (1.6)	0 (0.0)	
Mortality					
Mortality secondary to ESKD	8 (4.02)	4 (5.3)	4 (6.2)	0 (0.0)	

Proteinuria ≥300 mg/L. Hematuria >10 HPF. Hypertension >95th percentile for age, gender, and height; CKD, worsening eGFR <60 ml/min/1.73 m²; end stage kidney disease, eGFR <15 ml/min/1.73 m². DVS: dysfunction voiding syndrome, NB: neurogenic bladder due to spinal dysraphism, VBS: valve bladder syndrome, SD: standard deviation, Max: maximum, eGFR: estimated glomerular filtration rate, RRT: renal replacement therapy, VUR: vesico-ureteral reflux, DMSA: di-mercapto-succinic acid, DTPA: diethylenetriamine penta-acetic acid, MAG3: technetium 99 mercapto-acetyl-triglycine scan, CIC: clean intermittent catheterization, CKD: chronic kidney disease

Hinman's syndrome) was the most frequent group in our cohort. This is different from our previous study in 2006, when neurogenic bladder secondary to spina bifida was the main underlying etiology of bladder dysfunction.¹⁰ Neuro-spinal dysraphism was also reported by others as the most common cause of neurogenic bladder.^{2,11} This difference could be explained by better awareness and early diagnosis of DVS and a reduction in the

incidence of spinal dysraphism after implementation of folic acid fortification program.¹² Hinman's syndrome (previously known as non-neurogenic neurogenic bladder) was first described by Hinman and Baumann¹³ as an entity of bilateral/unilateral hydronephrosis, vesicoureteral reflux, and bladder trabeculation. It results from detrusor/sphincter dyssynergia with an inability to relax the sphincter muscle, while attempting

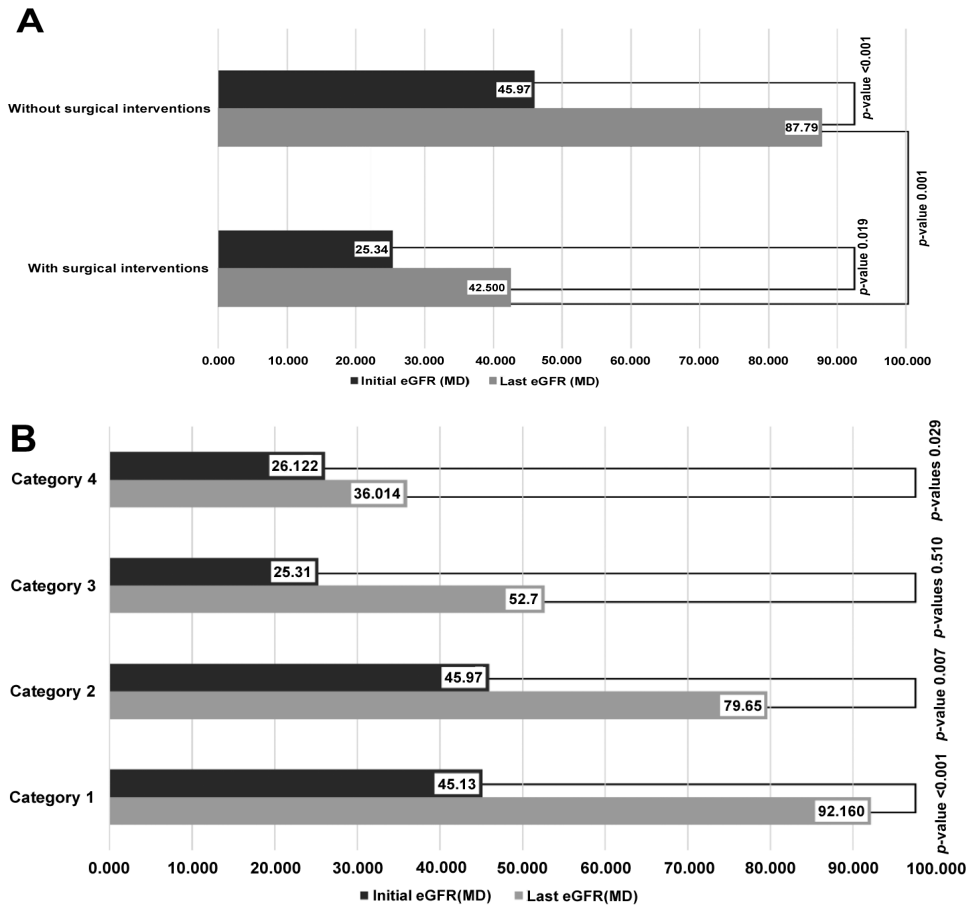


Figure 2 - A) Comparison between the median of estimated glomerular filtration rate test (eGFR) for the surgical and non-surgical patient's group. B) Comparison between the initial and last follow up median eGFR with regards to different management. Category 1: 62 children who did not need clean intermittent catheterization (CIC) or surgery, Category 2: 50 children who needed CIC but did not need surgery, Category 3: 25 children who have surgery but they did not need CIC, Category 4: 62 children who did need both CIC and surgery. *significant value ($p < 0.05$).

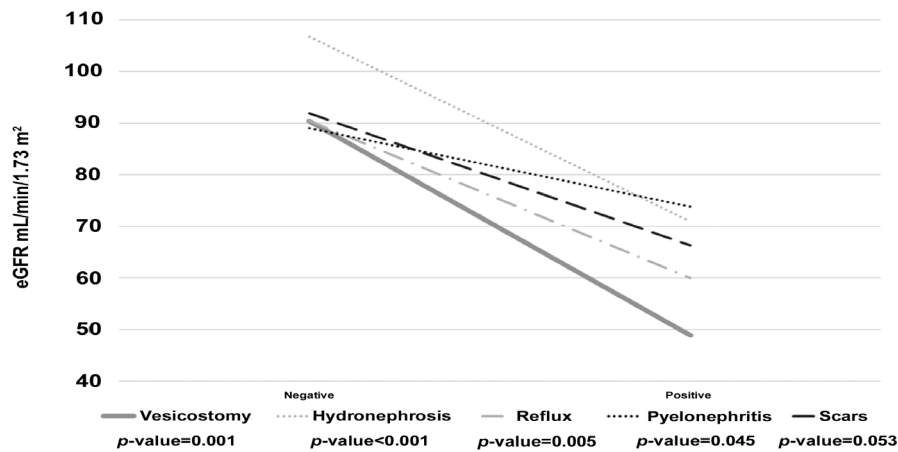


Figure 3 - Comparison of different variables depends to the last follow up estimated glomerular filtration rate test.

to void voluntarily, associated with bladder wall thickness and bladder outlet obstruction, VUR, and progressive hydronephrosis.¹⁴ The median age at presentation of DVS in our cohort was 48 months, although 25 (33%) were presented early in infancy. This is consistent with the previous belief that it represents a disorder of older aged children. Few case series have reported a severe form of dysfunctional voiding in newborns with no evidence of anatomical obstruction or neurological pathology.^{6,15} Non-neurogenic bladder and dysfunctional voiding are major risk factors for VUR, UTI, and renal damage.¹⁶ The presence of VUR in children with voiding dysfunction increases UTI and renal damage.¹⁷ This is similar to our observation that VUR, hydronephrosis, pyelonephritis, and renal scarring are more common in DVS group and have negative impact on the last eGFR.

Neuropathic bladder in children has a wide spectrum of congenital or acquired causes. The goals of management regardless of the etiology are maintaining low intravesical pressure, normal bladder compliance, preservation kidney function, and prevention of upper urinary tract damage. Thirty-two percent of our cohort had neuropathic bladder, the median age at presentation was 24 months, this is a quite younger age compared to our previous studies.^{10,18} Most children in this group had preserved normal kidney function, reflecting better awareness of nephro-urology care in those children. This is consistent with other recent reports that children born with spina bifida can possibly use their own kidneys for their entire lifetime.¹⁹ Management of NB requires patient education, timed voiding, CIC, indwelling urinary catheter, and urethral or bladder surgical procedures.²⁰ Approximately, 56.8% of our cohort was managed with CIC and oral anticholinergics (61.6%) according to the recommendation.²¹ Clean intermittent catheterization is the recommended method of bladder management for patients with NB with complete or partial urinary retention, as bladder evacuation reduces intravesical pressure, making the bladder mucous membrane more resistant to infectious bacteria as it improves blood circulation in the bladder wall.²²

Thirty percent of our cohort have VBS, 43% have evidence of CKD at presentation, and 36% have progressed to ESKD. This could be explained by the renal dysplasia that associate PUV and is reflected on high nadir creatinine level. Previous reports showing nadir creatinine is an important predictor of outcome in children with VBS.^{23,24} Valve bladder syndrome is a complication of PUV, resulting in a combination of hypertrophy of the bladder walls, persistent upper urinary tract dilatation, hydronephrosis and

vesicoureteral reflux.²⁵ We previously studied 68 boys who underwent endoscopic fulguration of PUV, the incidence of bladder dysfunction was 52.9%, and 58.8% had secondary VUR.²³ Peters et al,²⁶ showed urodynamic in 75% of VBS children revealed bladder instability, poor compliance, and myogenic failure. Posterior urethral valves is usually managed by endoscopic urethral valve ablation after birth, but in preterm neonates with extremely small urethras, temporary vesicostomy may be necessary.²⁷ Vesicostomy is an incontinent, supra sphincteric urinary diversion that maintain a low-pressure urinary system. Twenty percent of our cohort had vesicostomy as a primary surgical management. This high rate could be explained by surgeon and parent's preference, as children would not need CIC.

We observed patients who needed vesicostomy had significantly lower last follow up median eGFR when compared with the rest. Similarly, Close et al,²⁵ reported more frequent bladder dysfunction in patients with PUVs and in children with ureterostomy or vesicostomy after unsuccessful valve ablation. Other's studies are showing bladder do regain normal function after a period of defunctionalization caused by vesicostomy.^{24,28}

Augmentation cystoplasty is used to increase bladder capacity, reduce intravesical pressure, and preserve renal function. In our study, ilio-cystoplasty was carried out in 24 children and 6 have mitrofanoff or monti procedure with no reported major complications and experienced fair preservation of kidney function. Similarly, Mehmood et al,²⁹ assessed the factors predicting kidney function outcome after augmentation cystoplasty in 41 children, and found the augmentation cystoplasty was not the cause of the progression to ESKD in patients with renal impairment. While Husmann et al,³⁰ studied the long-term complications following bladder augmentations in 75 patients with spina bifida, deterioration in renal function has been observed in 15%. Others observed complications included bladder calculi, recurrent pyelonephritis, and spontaneous bladder perforation.

Injection of botulinum toxin (BTX-A) into bladder wall was indicated in 4 (2%) children of our cohort as an adjuvant treatment of overactive bladder, despite the use of oral anticholinergics, for this small number, we could not statistically conclude the benefits of this procedure in pediatric patients; however, Marte et al,³¹ concluded that BTX-A represents a viable treatment of NB secondary to meningomyelocele, with satisfactory results when anticholinergic agents are not effective or when their side effects lead the patient's non adherence to the treatment.

In the present study, 11.5% of patients were commenced on RRT. In a previous observational retrospective study from our center in 2015, 1000 children with CKD were enrolled, the incidence of RRT was 7.7% (hemodialysis 3.6%, peritoneal dialysis 2.6%, and kidney transplantation 1.5%), and bladder dysfunction was the most frequent cause of obstructive uropathy (12.1%).³² McLeod et al,³³ reported in a multicenter study, 274 children with PUV, who were treated before 90 days and were treated for a median of 6.3 years, 16% progressed to ESKD and required RRT by 10 years of age.

A pediatric kidney transplantation program is not available in our hospital, and we have to refer patients to other centers with considerable difficulty. Saeed et al,³⁴ reported that pediatric kidney transplantation rate in most Arab countries was 0.87 per million and it relied exclusively on living donors. While in developed countries, the rate mostly ranges from 5-10 per million. He concluded that the lack of well-developed deceased donor programs was the main issue that needed to be addressed.

Study limitations. A single-center, retrospective design and has a relatively small sample size in each group. However, our results reflect the improved awareness and management of bladder dysfunction in children over the last decade. Further studies are needed in the era of elimination dysfunction, especially among the dysfunction voiding syndrome in early infancy.

In conclusion, voiding dysfunction is an important cause of CKD children. Early diagnosis and management are associated with better prognosis. Pyelonephritis, VUR, hydronephrosis and renal scarring have negative impact on the preservation of kidney function. Children managed conservatively have better prognosis than those who needed surgical intervention.

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