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Original Research Article

Ten years institutional experience with study of prognostic factors affecting renal outcome in children with posterior urethral valves

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ABSTRACT

Background: Evaluation of our 10 years' experience and analyze the prognostic factors affecting renal outcome in children with posterior urethral valves (PUV).
Methods: We retrospectively reviewed the medical records of 129 patients diagnosed and managed as posterior urethral valves from 2009 till 2019 in our institution age of presentation, signs and symptoms, anthropometry, surgical interventions, and biochemical investigations were recorded and data were analyzed on an excel spreadsheet.
Results: Mean age of presentation was 3 years and mean follow up was 4 years. 99 underwent primary valve ablation and 30 patients underwent diversion as primary treatment, the most common presenting symptom was poor urinary stream (90), enuresis (88), and fever (60). Correlation of resolution of symptoms pre and postoperatively was statistically not significant. 26% patients developed chronic renal failure (CRF) and 8.5% patients progressed to end stage renal disease (ESRD). Correlation of mean nadir serum creatinine >1 mg/dl (p=0.030), presence of protenuria (p=0.020), bladder dysfunction (p=0.029), bilateral high grade vesicoureteric reflux (VUR) (p=0.019), hypertension (p=0.01) was statistically significant. Correlation of age of presentation (p=0.341), outcome for patients treated with diversion or valve ablation in relation to CRF (p=0.239), incontinence (p=0.209), malnutrition (p=0.194) was statistically insignificant.
Conclusions: Nadir serum creatinine >1 mg/dl, presence of protenuria, bladder dysfunction, bilateral high grade VUR are significant prognostic factors affecting long term outcome in PUV. Early detection and timely management may lead to a better outcome in these patients.

Keywords: Posterior urethral valves, Prognostic factors, Chronic renal failure, Nadir serum creatinine, Bladder dysfunction

INTRODUCTION

Posterior urethral valve (PUV) is the commonest cause of obstructive uropathy in male infants with an estimated incidence of 1:25,000 live births and 1:5000 male infants.[1] Early diagnosis and intervention to decrease bladder pressure and stabilize the upper urinary tract are important to delay or prevent the progression of renal insufficiency. The incidence of chronic renal failure (CRF) was 34% and end stage renal disease (ESRD) was 10% at the end of 10 years, and the incidence increased to 51% having CRF and 38% having ESRD at 20 years.[1] Various factors like age at presentation, nadir serum creatinine greater than 1.0 mg/dl, vesicoureteric reflux (VUR) grade 3 or higher at diagnosis, recurrent febrile UTIs, renal dysplasia and bladder dysfunction have been associated with long-term poor prognosis.[2-4] These prognostic factors can help in planning management and serve as a guide in parental counselling. The aim of this study was to report our long-term renal outcome and analyze these prognostic factors in the management of children with posterior urethral valves.

METHODS

We retrospectively reviewed the medical records of 129 patients diagnosed and managed as posterior urethral valves from 2009 till 2019 in our institution. The details of children with regard to the age, presenting symptoms, presenting and nadir serum creatinine, as well as information on prenatal ultrasound and postnatal abdominal ultrasound, presence or absence of VUR at diagnosis and surgical interventions done were obtained from records. The presence of hypertension (systolic and/or diastolic blood pressure >95 mmHg weight, for gender, age and height), malnutrition (weight for age <-2 standard deviation, according to the WHO classification) were recorded.[5] The reports of ultrasonography, micturating cystoure throgram (MCU), dimercaptosuccinic acid scan, diethylenetriamin-epentaacetic acid scan done at initial workup and later in follow-up were recorded. History of urinary tract infection and severe bladder dysfunction requiring clean intermittent catheterization was also noted. The data were entered into an excel spreadsheet and analyzed using descriptive statistics.

Treatment protocol

On admission basic renal function tests, including blood urea nitrogen, serum creatinine, venous blood gas analysis, serum electrolytes, as well as urinary ultrasonography were performed, After stabilizing the patients by controlling infection, correction of fluid, electrolyte balance and initial catheter drainage, patients were subjected to voiding cystourethrography and taken for primary valve fulguration. After the valve fulguration indwelling catheter was kept for 48 hours. After this result of primary valve ablation was being assessed by observing urinary stream and per abdominal examination patients were then subsequently discharged on antibiotic prophylaxis. Urinary diversion was done in patients with persistent fever, sepsis, renal impairment with acidosis and dyselectrolytemia not responding to catheter drainage and parenteral antibiotics.

Follow up protocol

Patients were followed up in an outpatient clinic for every 3 months in the first year, at 6 months intervals for the next 4 years and yearly afterward. At each follow-up, weight, height, serum creatinine, and full blood count and urine culture, complications developed were also noted. Ultrasonography of abdomen was done to assess renal growth, asymmetry, presence of residual hydronephrosis and bladder residual volume. Bladder function was assessed by the history of dribbling and significant residual urine on ultrasound in those children without VUR. MCU was also performed in all children at 3month follow-up to confirm the adequacy of valve ablation; cystoscopy was done only in children with abnormal MCU results. Urodynamic studies were undertaken only in select patients with voiding dysfunction, persistently high serum creatinine, or persistent hydroureteronephrosis.

RESULTS

A total of 129 boys with posterior urethral valves (PUV) were diagnosed and treated in our institution from 2009 to 2019. Mean age of presentation was 3 years (0-14 years) and mean follow up was 4 years (1-10 years). Out of these 27 (21%) patients were antenatally diagnosed. Overall, 34 (26%) patients developed chronic renal failure (CRF) and 11 (8.5%) patients progressed to end stage renal disease (ESRD). Age of presentation was less than 1 year in 61% and incidence of CRF was 22.7% on follow up. 38.7% was presented at more than 1 year of age and incidence of CRF was 32%. This was statistically insignificant as shown in (Table 1).

Table 1: correlation of age of presentation of PUV with CRF.

Age of presentation (year)	N (%)	CRF (%)	P value
<1	79 (61.2)	18 (22.7)	0.341
>1	50 (38.7)	16 (32)	

Out of 129 patients 99 underwent primary valve ablation and 20 patients underwent ureterostomy and 10 patients underwent vesicostomy. The most common presenting symptom was poor urinary stream and dribbling in 90 patients and postoperatively on follow up in 30 patients followed by fever with UTI in 60 patients and postoperatively on follow up in 10 patients, nocturnal enuresis in 40 patients and postoperatively on follow up in 20 patients, diurnal enuresis in 44 patients preoperatively and postoperatively on follow up in 25 patients. Correlation of resolution of symptoms pre and postoperatively was statistically not significant as shown in (Table 2).

Table 2: Patient characteristics before and after primary treatment of posterior urethral valves.

Variables	Before valve fulguration	After valve fulguration	P value
Poor urinary stream	90	30	0.452
Nocturnal enuresis	40	20	0.089
Diurnal enuresis	44	25	0.097
Fever	60	10	0.223

The mean nadir serum creatinine (after removing the obstruction for minimum of 5 days) >1 mg/dl was seen in 94% patients who progressed to chronic renal failure on follow up which was statistically significant (p=0.030). The appearance of proteinuria was also statistically

significant (p=0.020) with 78% of boys with CRF had proteniuria compared to 33% of with normal renal function on follow up. Bladder dysfunction categorized as unstable low compliance or myogenic failure or need of CISC was seen in 67% of patients with CRF, the presence of hypertension was seen in 58% of patients with CRF and bilateral grade 4 or more VUR on MCU studies was seen in 61% of patients with CRF. All these risk factors were statistically significant as shown in (Table 3).

Table 3: Comparison between patients with normal renal function and with chronic renal failure.

Variable	Normal renal function (n=95), frequency (%)	Chronic renal failure (n=34), frequency (%)	P value
Mean nadir serum creatinine >1mg/dl	25 (26)	32 (94)	0.030
Protenuria	32 (33)	25 (78)	0.02
Hypertension	25 (26)	20 (58)	0.01
Bladder dysfunction	30 (31)	23 (67)	0.029
Bilateral high grade VUR	26 (27)	21 (61)	0.019

Table 4: Sequel of PUV in each treatment group during follow up.

	Valve ablation (n=99), frequency (%)	Diversion (n=30), frequency (%)	P value
Chronic renal failure	20 (20)	14 (46)	0.239
Incontinence	18 (18)	11 (36)	0.209
Malnutrition	10 (10)	8 (26)	0.194

On follow up among the 99 patients with primary valve ablation 20 patients progressed to CRF and 14 patients of the diversion (vesicostomy and ureterostomy) progressed to CRF. Incontinence requiring clean intermittent self catherisation (CISC) was noticed in 18 patients with valve ablation and in 11 patients with diversion. 10 boys with primary valve ablation and 8 patients with diversion had moderate to severe malnutrition. These sequel of PUV in each treatment group was statistically insignificant as shown in (Table 4).

The most common surgical procedure during follow up period was redo valve ablation. Further surgical procedures during follow up are summarized in (Table 5).

Table 5: Further surgical procedure after primary treatment during follow up.

Surgical procedure	Valve ablation (n=99)	Diversion (n=30)
Redo valve ablation	80	28
Ureteric reimplantation	21	22
Augmentation cystoplasty	5	2
Mitrafinoffs procedure	8	3

DISCUSSION

Posterior urethral valves are the commonest cause of urethral obstruction in a male child. Management and assessment of outcome of treatment in patients with PUV have undergone a great deal of change since the condition was first described. Despite improvement in short term survival of these patients nearly two thirds will develop CKD and nearly 38% eventually progress to ESRD at the end of 20 years.[1] The prognosis can be improved if the anomaly is tackled soon after diagnosis and the factors that affect the prognosis are identified and timely managed. Morbidity in terms of recurrent urinary tract infection (UTI), deteriorating renal functions, and growth failure may be reduced by timely and aggressive interventions which involves surgery, pharmacology, and clean intermittent catheterization (CIC). In our study we have analyzed these prognostic factors in the management of our patients.

Age at presentation has been suggested as a predictor of renal function in children with PUV. Reinberg et al reported that patients diagnosed with PUV in utero have the worst prognosis.[6] Bomalaski et al demonstrated that late presentation was associated with an additional 10% risk of end-stage renal disease (ESRD).[7] Meguerian et al found that age at presentation was not a significant factor as renal failure developed in 14.7%, 14.3% and 10% of patients diagnosed at less than 1 month of age, between 1 month and 1 year, and in those over 1 year of age at presentation, respectively.[8] In our study the incidence of CRF was 22.7% in <1 year of age and 32% in >1 year of age and was not statistically significant. The major symptoms at follow-up were enuresis (nocturnal and diurnal) and dribbling. In a study by Lal et al 35% had symptomatic voiding dysfunction, the most common symptom being nocturnal enuresis with diurnal urgency and frequency on long term follow-up.[9] In the study by Connor et al 19% patients had urinary incontinence on follow-up.[10] These symptoms are due to the poor

concentrating ability of the renal tubules along with poor bladder compliance.

In current study it was observed that nadir serum creatinine greater than 1 was strongly associated (p=0.030) with incidence of CRF. Our results coincide with Reinberg et al who documented that a nadir serum creatinine higher than 1.2 mg/dl in the first year of life was predictive of renal failure.[6] Williams et al also found that a return of serum creatinine to less than 1 mg/dl is predictive of a favorable outcome.[11] Similarly to other studies in our study the appearance of protenuria was associated with worse prognosis.[12] Pathogenically this result could be related to hyperfiltration by the functioning nephrons in their attempt to maintain a normal renal function producing proteinuria and focal segmental glomerulosclerosis. As also seen in our study bladder dysfunction has an immense impact on long term renal outcome. Bauer et al first described the five types of bladder function in cases of PUV.[13] Among these poor compliance and myogenic failure are the patterns associated with the worst outcome for renal function.[14] The role of VUR in PUV is still controversial. Some authors consider that unilateral VUR has no relation with the prognosis of CRF and bilateral high-grade reflux is significantly correlated with the poor prognosis.[2,9] In current study the correlation between bilateral high grade VUR and CRF was statistically significant.

In the recent decades, primary endoscopic valve ablation has become the mainstay of treatment in PUV cases. Urinary diversion is considered in patients with persistent fever, sepsis, renal impairment with acidosis and dyselectrolytemia not responding to catheter drainage and parenteral antibiotics. Urinary diversion has the potential to improve renal function in the short term by draining the pelvicaliceal system and can defer renal replacement to a later stage but there is no convincing evidence to support its role in long term progression to CRF as these patients are born with renal dysplasia secondary to abnormal caudal budding of the ureter from the mesonephric duct with subsequent abnormal induction of the mesenchyme. In current study we did not find any statistical significant difference of the outcome for patients treated with diversion or valve incision. Similarly in a study from the hospital of Philadelphia comprising 100 patients showed no difference in the incidence of CRF in patients who were treated by primary resection (74%), vesicostomy (13%), and high urinary diversion (9%) in a follow up of 10-20 years.[15] When comparing primary valve ablation with primary vesicostomy, Godbole et al found no significant difference in serum creatinine and management of posterior urethral valves in the glomerular filtration rate (GFR) at 1 year of between the two groups.[16]

In our study 26% patients developed CRF and 8.5% patients progressed to ESRD in a 10 year follow up. Smith et al in a series of 100 patients with PUV described an incidence of 10% and 38% and 34% and 51% at 10 and 20 for CKD and ESRD, respectively.[17] Warren et al reported an incidence of 23% and 11% for CKD and ESRD, respectively, at a follow-up of 8.3 years (1 month to 18 years).[18] In current study moderate to severe malnutrition was seen in 14% patients on follow up of ten years. In a study by Tejani et al with a mean follow-up of nine years, growth failure was present in 40% of patients.[19] Uthup et al also reported growth failure in 30-40% of children with PUV.[20]

CONCLUSION

Nadir serum creatinine >1 mg/dl, presence of protenuria, bladder dysfunction, bilateral high grade VUR are significant prognostic factors affecting long term outcome in PUV. Early detection and timely management may lead to a better outcome in these patients.

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