MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2024.2.18.593.598

Clinico-Therapeutic Analysis of Posterior Urethral Valve in Children: A Hospital Based Retrospective Study from Eastern India

[1]Imran Khan, [2]Anindya Pradhan, [3]Indrani Ghosh, [4]Indranil Chatterjee and [5]Aritra Kapat

[1]Department of Physiology, LN Medical College, Bhopal Madhya Pradesh 462042, India

[2]Department of Paediatric Medicine, Dr B C Roy Post Graduate Institute of Paediatric Sciences, Kolkata West Bengal 700054, India

[3]Department of Paediatric Medicine, Medical College And Hospital, Kolkata, West Bengal 700073, India

[4]Department of Paediatric Surgery, Dr B C Roy Post Graduate Institute of Paediatric Sciences, 111, Narkeldanga Main Road, Phoolbagan, Kankurgachi, Kolkata, West Bengal, Pin: 700054, India

[5]Department of Paediatric Medicine, Dr B C Roy Post Graduate Institute of Paediatric Sciences, 111, Narkeldanga Main Road, Phoolbagan, Kankurgachi, Kolkata, West Bengal, Pin: 700054, India

ABSTRACT

Management of posterior urethral valve (PUV) is a challenge to pediatric surgeons due to its late presentation and sequlae despite optimum treatment, which needs a long term follow-up. The aim of the study is to describe the presentation, therapeutic management and eventual outcome in cases of posterior urethral valve. It is a hospital-bound time-framed retrospective analysis based on digitalized hospital records of the past 10 years, which included postoperative PUV patients. A total of 40 cases were analyzed. 7.5% of cases were antenatally detected. The mean age of presentation was 8.92±6.27 months. The major presenting symptom was post micturition dribbling, followed by poor urinary stream. 30% of cases needed medical management with alpha blockers. Repetitive urethral valve fulgration was required for 27.5% of the patients, whereas 25% patients needed draining procedures. Vesicostomy was done in 17.5% cases and ureterostomy was done in 7.5% cases. Postoperatively, there was significant improvement in vesicoureteric reflux, with 82.5% of patients showing no signs of reflux. 75% of patients had creatinine more than 1 mg dL^{-1} preoperatively and postoperative change in serum creatinine was statistically insignificant ($F_{2,117} = 2.50$, $p = 0.086$). The structural ultrasonographic bladder parameters also didn't change significantly postoperatively; rather, they decreased gradually on long-term follow-up. A timely evaluation and apt management are required for cases of PUV. Despite optimum management, the disease imparts some long-standing deleterious effects on the bladder and kidney, which often lead to end-stage renal diseases, which prompt regular, periodic follow-up.

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Key Words
Urethra, vesicoureteric reflux, kidney failure, ureterostomy

Corresponding Author
Aritra Kapat,
Department of Paediatric Medicine, Dr B C Roy Post Graduate Institute of Paediatric Sciences, 111, Narkeldanga Main Road, Phoolbagan, Kankurgachi, Kolkata, West Bengal, Pin: 700054, India

Author Designation
[1]Assistant Professor
[2,3,5]Senior Resident
[4]Professor

Received: 24 May 2024
Accepted: 18 June 2024
Published: 23 June 2024

Citation: Imran Khan, Anindya Pradhan, Indrani Ghosh, Indranil Chatterjee and Aritra Kapat, 2024. Clinico-Therapeutic Analysis of Posterior Urethral Valve in Children: A Hospital Based Retrospective Study from Eastern India. Res. J. Med. Sci., 18: 593-598, doi: 10.59218/makrjms.2024.2.18.593.598

INTRODUCTION

Posterior urethral valve (PUV) is the commonest cause of lower urinary tract obstruction in male infants, with an estimated incidence of 1:5000 male infants[1], although a much rarer incidence rate of around 1/25000 has been demonstrated in some medical literature[2]. Posterior urethral valve (PUV) has a broad spectrum of clinical presentation, disease severity and associated sequelae[3]. Progressive renal deterioration is not uncommon and 25-40% of PUV patients develop renal failure at varying ages and in addition to that, some children also develop bladder dysfunction and growth retardation. The exact causative factor that may lead to the development of the PUV and associated bladder, renal and ureteric abnormalities has not been elucidated but it may appear to be multifactorial and may include a combination of teratogenic and gene mediated embryopathy. Development of end-stage renal disease (ESRD) shows a bimodal distribution. The initial peak may be due to inherent renal dysplasia, whereas the second late peak is due to progressive bladder dysfunction. The most common clinical presentation is urinary symptoms (poor urinary stream and dribbling of urine) along with severe septicemia, abdominal distension, respiratory distress and failure to thrive[4]. While there is no control over the developmental renal dysplasia, a better understanding of the bladder behavior and its appropriate management could prevent the deleterious long-term problems in these children. There is now wide acceptance that maximizing the long-term outcome in PUV patients centers on optimizing bladder function. Initial management of all patients with posterior urethral valves requires immediate establishment of urinary catheter drainage followed by vesicostomy or pyelostomy. Given the rarity of PUV, most medical professionals do not encounter many PUV cases and few units have good experience in treating them. Early diagnosis, early referral to pediatric urological centers, improved instrumentation and a close follow-up significantly decrease mortality and morbidity[5]. Paediatric surgeons and urologists treating PUV patients as children do not meet them in adulthood. Long-term outcomes of PUV cases are not properly known as systematic follow-up studies are lacking. Here we present a retrospective analysis in patients of posterior urethral valve to evaluate the various clinical presentations, investigations, surgical interventions, complications and long term outcome.

MATERIALS AND METHODS

This is a hospital-bound, time-framed retrospective study of observational analytical design conducted in a span of 1 year in Apollo Multi-Speciality Hospital, Kolkata. All operated children for PUV attending hospital pediatric and urology clinics for follow up have been enrolled in the study and their preoperative hospital records were thoroughly checked based on their unique hospital-based health identity number. Total data spanning the past 10 years was collected and patients were also summoned with all their health records from their contact information whenever needed. Children with spinal dysraphism were excluded from the study. Detailed information regarding clinical profile, medications used, renal ultrasound (RUS) findings, creatinine levels, pre- and postoperative VUR status, presence or absence of urinary tract infections (UTIs) and surgical interventions was collected. Anthropometrical parameters like weight and height for age were plotted on the WHO growth chart.

Statistical analysis: Statistical analysis was performed with the help of Epi Info™ 7.2.2.2, which is a trademark of the Centers for Disease Control and Prevention (CDC). Using this software, basic cross-tabulation and frequency distributions were prepared. A chi-square test was used to test the association between different variables under study. A student t-test was used to test the significant difference between means. Also, one-way analysis of variance (ANOVA) followed by post hoc Tukey's test was performed with the help of critical difference (CD) or least significant difference (LSD) at 5 and 1% levels of significance to compare the mean values. $p<0.05$ was considered statistically significant.

RESULTS

In the study period, data of 40 patients with postoperative PUV were fully traced. The mean age at presentation (± standard deviation) of the patients was 8.92±6.27 months with a range of 1-42 months and the median age was 6 months. Most of the patients belonged to age <1 years (85.0%). Preoperative baseline characteristics are tabulated in Table 1. Regarding surgical intervention, it is evident from Table 1 that repetitive urethral valve fulgration was required for 27.5% of the patients and lately most of the patients (75.0%) didn't require draining procedures; among them, a vesicostomy was done in 7 patients.

The mean age of patients in the diversion group (n = 10) was 3 months as compared to the non-diversion group (n = 30), where the mean age was 10.8 months. Postoperatively, there was significant improvement in vesicoureteric reflex, with 82.5% of patients showing no signs of reflux (Fig. 1). Table 2 summarizes the preoperative and postoperative distribution of vesicoureteric reflux.

Table 1: Summary of pre-operative baseline characteristics and operative procedures in patients with posterior urethral valve

Parameters	Observed values in the study group (N = 40)
Mean age (months)	8.92±6.27
Age group at presentation (months)	
1-5	18 (45%)
6-12	16 (40%)
>12	06 (15%)
Antenatally diagnosed	03 (7.5%)
Pre-operative height (cm)	80.85±28.95
Pre-operative weight (kg)	12.30±11.79
Clinical presentation	
Urinary dribbling	30 (75%)
Poor stream	29 (72.5%)
Urinary tract infection	25 (62.5%)
Pre-operative serum creatinine (mg dL^{-1})	1.77±1.96
Pre-operative medicine trial	12 (30%)
Terazosin	09 (22.5%)
Oxybutynin	03 (7.5%)
Repeat fulgaration	11 (27.5%)
Draining procedure	10 (25%)
Vesicostomy	07 (17.5%)
Ureterostomy	03 (7.5%)

Table 2: Preoperative and Postoperative distribution of radiological parameters in patients with posterior urethral valve

Parameters	Pre-operative	Postoperative at 6 months
Vesicoureteric reflux		
No reflux	06 (15%)	33 (82.5%)
Grade 1	08 (20%)	04 (10%)
Grade 2	12 (30%)	
Grade 3	08 (20%)	
Grade 4	04 (10%)	
Grade 5	02 (5%)	03 (7.5%)
USG parameters		
Pelvic dilatation >10 mm	27 (67.5%)	35 (87.5%)
Ureteric dilatation	26 (65%)	35 (87.5%)
Bladder wall thickening	24 (60%)	33 (82.5%)
Trabeculation	26 (65%)	35 (87.5%)

One way ANOVA showed that there was a significant difference in mean weight of the patients at different times ($F_{2,117} = 4.02$, $p = 0.0226$). As per Tukey's critical difference followed by ANOVA, the mean weight of the patients increased significantly over time. A total of 14 (35%) patients were having failure to thrive preoperatively, 12 (30%) of patients were having failure to thrive postoperatively at 6 months and 13 (32.5%) were having failure to thrive postoperatively at their last visit. It also showed that there was a significant difference in mean height of the patients at different times ($F_{2,117} = 7.15$, $p = 0.0011$). As per Tukey's Critical Difference followed by ANOVA, the mean height of the patients increased significantly over time. A total of 75% of patients had creatinine values more than 1 mg dL^{-1} at the time of presentation and postoperatively, by 6 months, a return of creatinine levels below 1 mg dL^{-1} was seen in 60% of patients, followed by 52.5% of patients having serum creatinine levels more than 1 mg dL^{-1} at their last contact in the study. This postoperative change in serum creatinine was statistically insignificant ($F_{2,117} = 2.50$, $p = 0.086$) and the significant rise in creatinine despite the surgical intervention is the proof that the surgery is not curative and eventually end stage renal disease will set in (Fig. 2).

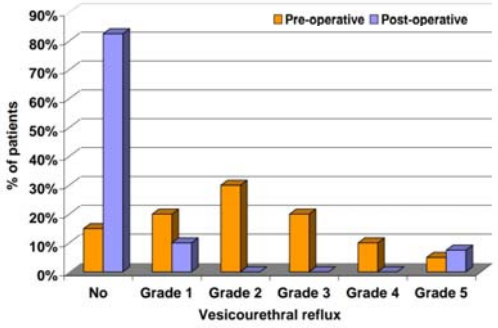

Fig. 1: Distribution of pre and post operative vesicoureteric reflux of the patients

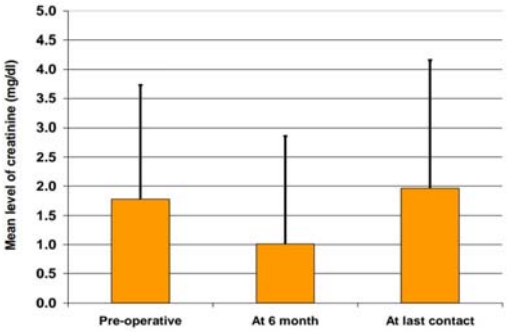

Fig. 2: Comparison of level of creatinine at different timeline

Table 2 summarizes the postoperative ultrasonographic bladder parameters from which it was evident that pelvic dilatation, ureteric dilatation, bladder wall thickening and diverticulae persisted despite surgery and this persistence was statistically significant in each case at a p-value of 0.001. Those structural changes seemed to decrease on long follow-up, with a distribution of 72.5, 70, 52.5 and 70%, respectively, at their last follow-up.

DISCUSSION

This hospital based retrospective study was carried out on post operated PUV (posterior urethral valve) patients presenting to a private, tertiary care hospital. A total of 40 patients were included in the study. This study is intended to identify the complications, their risk factors and the long-term outcome for postoperative PUV patients. As per other clinical studies showing 50 to 70 percent of boys with posterior urethral valves generally seen in the first year of life and 25-50% are initially presented during the neonatal period[6]. In our study, the mean age group of presentation was 8.92±6.27 months. The exact etiology of posterior urethral valves is unknown. PUV is most commonly sporadic. However, few familial cases have been reported in two successive generations, in the siblings and in the identical and fraternal twins, which suggests some form of genetic background[7].

In the present study, repeat fulgration was required for 11 out of 40 patients. This constitutes 27.5% of all the patients with PUV in our study. In other studies, residual valves requiring second ablation of PUV have been reported in 1-29% of patients and the data is in accordance with our study[8]. For most of the patients (75.0%) of PUV, only fulgration was done alone and no other procedure was required . Out of 25% patients for whom draining procedure was required, the proportion of vesicostomy (17.5%) was significantly higher than that of ureterostomy (7.5%). The mean age of patients in the diversion group was 3 months as compared to the non-diversion group, where the mean age was 10.8 months. A diversion procedure was required for critically ill and severe cases and premature infants mostly. 40% of patients with diversion procedures were 1 month of age only. Recent studies found that pediatric urologists mostly prefer endoscopic valve resection as the preferred method for operating posterior urethral valves[8,9]. Urinary diversion is useful in critically ill patients with resistant urinary infection and patients with increasing plasma creatinine values after valve ablation[10]. Justification for urinary diversion for improving overall renal function and prognosis in a few particular cases was confirmed with many studies[11].

PUV are accompanied by VUR, with incidences usually between 26 and 72%[3]. VUR in PUV patients is considered to be secondary to the increased infravesical pressure and loss of ureterovesical junction competence[9]. The well-established grading system adopted by the International Reflux Study Committee (IRSC) is based on the classification system originally presented. Grade I visualizes the escape of the contrast medium into the ureter only and grade II into an anatomically normal pyelocalyceal system. Grade III constitutes reflux to the dilated collecting system and in grade IV there is more pronounced dilatation with the blunting of the calyces and the tortuosity of the ureter. Grade V represents massive reflux with gross dilatation and deformation of the collective system and ureter[12]. Regarding postoperative VUR in our study, a total of 8 patients from grade III VUR (pre-op) were having complete improvement (grade 0 VUR) and 1 patient (12.5%) was having grade I VUR. Out of 4 patients with grade IV VUR , 3 patients (75%) had grade I VUR and 1 patient (25%) developed grade V VUR postoperatively. 2 patients were having VUR grade V both pre- and postoperatively. Grade I and grade II VUR patients were having complete improvement (grade 0 VUR) postoperatively. In other study series of Heikkilä *et al*.[13], VUR was found to resolve in 62% of patients at a median time interval of 1.28 (range 0.04-15.16) years after resection of the valve. Up to 50% of VUR may resolve spontaneously after treatment of the valves and following relief of infravesical obstruction. Similarly, in the present study, 85% of PUV patients were having VUR and 67.5% of the patients improved completely after surgery. 82.5% of the patients had no vesicoureteral reflux after surgery, which was significantly better than that of before surgery (15.0%). As VUR in PUV cases is presumably secondary to infravesical obstruction. So as expected, after valve ablation, resolution of VUR is seen.

In our study, 62.5% of the patients had UTI and 75.0% of the patients had the problem of dribbling during urination. 57.5% of the patients had the problem of straining during micturition along with a poor urinary flow stream in 72.5%. In one of the recent series[14], obstructive symptoms in the form of poor stream and dribbling were present in 76.6% of cases, which is in accordance with our study. The clinical findings of patients with PUV seen in other studies are poor urinary flow stream (73.33%) and dribbling during urination (73.33%)[15]. In the studies of Tambo *et al*.[16], dribbling during urination was the most common presenting symptom and recurrent UTI was present in 62%. In the present study, 35% of patients were having failure to thrive preoperatively, followed by 30% of patients having failure to thrive postoperatively at 6 months and 32.5% were having failure to thrive postoperatively at their last contact. This is in accordance with another study of Drozdz *et al*.[14], where on long term follow-up, normal growth status was achieved in 69% of patients in the treatment group with valve ablation and 20% in the treatment group with vesicostomy.

In our study, at the time of presentation, thickness of bladder wall was seen in 60% of patients, dilated ureter in 65% of patients and trabeculation of bladder in 65% of patients. A different study of Chatterjee *et al*.[15] found having a dilated bladder along with a thickened wall (40%) and a significant dilated posterior urethra as the commonest sonographic findings in patients with PUV, while a dilated posterior urethra with the filling defect in the posterior part of the urethra (60%) is the most common voiding cystourethrographic findings. In the present study, 75% of patients had creatinine values more than 1 mg dL^{-1} at the time of presentation and postoperatively, by 6 months, a return of creatinine levels below 1 mg dL^{-1} was seen in 60% of patients, followed by 52.5% of patients having serum creatinine levels more than 1 mg dL^{-1} at their last contact in the study. Similar findings were seen in the study of Chatterjee *et al*.[15], where serum creatinine levels were significantly higher in 80% of cases at the time of admission and in the postoperative period only 33% of patients were having levels of serum creatinine above the normal range. Another study of Tambo *et al*.[16] in their series reported that blood creatinine levels were

raised in 91% of their patients. At presentation, more than 95% of patients had increased blood creatinine values and after 1 month of follow-up, it was raised in 57% of patients and after 1 year of follow-up, 33% of patients had mean serum creatinine values higher than 2.9 mg dL^{-1}[14]. Another study of Sharma *et al*.[17] reported the occurrence of renal failure in 63% of their cases. In another study of Scott[18] of all the patients with decreased renal functions, return of normal renal function was seen in 60.6% of cases after treatment, which is consistent with the present study. Early age at presentation is mostly considered a risk for later renal failure. Diagnosis before the first year of life is a negative predictive factor of renal failure. Delayed presentation has been associated with a more benign clinical course than the early presentation[19]. In contrast, a number of studies from many institutions have revealed that impaired renal function is associated with delayed diagnosis or that there is no obvious difference among those diagnosed early or late[20]. It is a matter of concern that even after the early successful treatment of valves, these children continue to have persistent problems with a long-term morbidity that often result in end-stage renal disease (ESRD). It has been found that the incidence of chronic renal failure (CRF) was 34% and 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]. A recent study noted a clear prognostic relation between initial serum creatinine and future renal function after a mean follow-up of 4.4 years[8]. In contrast to that, in some recent studies they found no significant correlations with initial serum creatinine and progression to chronic renal failure[20]. From our study, it was found that serum creatinine levels at the time of presentation and during the period of the following months have a correlation with prognosis. Although some controversial data exists, this observation is in accordance with some earlier studies[21].

CONCLUSION

Posterior urethral valve is basically a dynamic disease process that continues to have lifelong effects on the bladder. Early presentation, poor primary renal function, high grade VUR and UTIs during infancy and early childhood carry the risk for deterioration of renal function followed by ESRD, which may be refractory to timely diagnosis and proper surgical interventions. Hence, these patients require long-term follow-up care for monitoring and treating the effects of altered bladder compliance.

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