

Posterior urethral valve: a retrospective review of cases and challenges of management in a low-resource centre.

Ajao E.A.¹, *Abiola O.O.², Alao A.M.³, Adeniran J.O.⁴

Resume

Objective: Posterior urethral valves (PUV) diagnosis and management remain a major challenge in developing countries. We sought to review cases of PUV managed in our health centre and to highlight the challenges in its management.

Methods: A retrospective analysis of patients with PUV managed over a 12month period. Data obtained from patients' medical records include: demography, clinical presentation, serum electrolytes, urea and creatinine, radiological diagnosis, initial management, surgical management and the outcome of management.

Results: Eight patients were managed during the period under review. The median age was 26 months. The commonest clinical feature was recurrent fever. Three patients (37.5%) had renal insufficiency requiring peritoneal dialysis at initial presentation. Six patients (75%) had Mohan's valvotomy while two (25%) died before valve ablation. One patient (12.5%) died a month after valve ablation from renal failure, while one (12.5%) had residual valve requiring a repeat valve ablation. Post-operative complication of urosepsis occurred in two patients (25%).

Conclusions: Physicians should have a high index of suspicion for PUV in boys who present with recurrent fever or urinary tract infections. Screening for foetal anomalies during routine ante-natal maternal ultrasonography will improve prenatal diagnosis of this condition.

Keywords: Low-resource centre, Management, Nigeria, Posterior urethral valve.

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Valve urétrale postérieure: examen rétrospectif des cas et des défis de la prise en charge dans un centre à faibles ressources.

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Resume

Objectif: Le diagnostic et la prise en charge des valves postérieures de l'urètre (PUV) restent un défi majeur dans les pays en développement. Nous avons cherché à examiner les cas de PUV gérés dans notre centre de santé et à mettre en évidence les défis de sa gestion.

Méthodes: Une analyse rétrospective des patients atteints de PUV pris en charge sur une période de 12 moi. Les données obtenues à partir des dossiers médicaux des patients comprennent: démographie, présentation clinique, électrolytes sériques, urée et créatinine. diagnostic radiologique, prise en charge initiale, prise en charge chirurgicale et résultat de la prise en charge.

Résultats: Huit patients ont été pris en charge pendant la période considérée. L'âge médian était de 26 mois. La caractéristique clinique la plus courante était la fièvre récurrente. Trois patients (37,5%) présentaient une insuffisance rénale nécessitant une dialyse péritonéale lors de la présentation initiale. Six patients (75%) ont eu la valvotomie de Mohan tandis que deux (25%) sont décédés avant l'ablation de la valve. Un patient (12,5%) est décédé d'un mois après l'ablation de la valvule d'une insuffisance rénale, tandis qu'un patient (12,5%) présentait une valvule résiduelle nécessitant une nouvelle ablation de la valvule. Une complication postopératoire de l'urosepsie est survenue chez deux patients (25%).

Conclusions: Les médecins doivent avoir un indice élevé de suspicion de PUV chez les garçons présentant une fièvre récurrente ou des infections des voies urinaires. Le dépistage des anomalies fœtales lors d'une échographie maternelle prénatale de routine améliorera le diagnostic prénatal de cette affection.

Mots-clés: Centre à ressources limitées, Management, Nigeria, Valve urétrale postérieure.

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INTRODUCTION

Posterior urethral valve (PUV) is the commonest cause of bladder outlet obstruction in male children (1,2). It occurs with reported incidence of 1 in 5,000 to 8,000 live male births (1,3). Despite its initial description by Morgagni in 1717 (3), PUV still remains a major cause of significant morbidity and mortality worldwide. Posterior urethral valve affects the development and function of the entire urinary tract more than any other urinary anomaly (4). It accounts for 20 to 40% of end stage renal disease (ESRD) in children (5). Presently, in most developed countries, about two-thirds of PUVs are diagnosed prenatally based on maternal ultrasound (3,6). However, in most parts of Nigeria, late presentation continues to be the norm. This adds to the challenges of management of the condition in this environment and more importantly, adversely impacts the outcome of management of these patients (7,8).

The aim of the study was to review the presentation, management, outcome and challenges in management of cases of PUV seen at a health centre in South west, Nigeria. This clinical audit will help to improve care and outcome of management of patients with PUV in a low resource settings through identification of changes needed to achieve an improved quality of care and outcome of management of patients with PUV.

METHODS AND MATERIALS

This was a 12months retrospective review (June 2016 to May 2017) of all PUV cases seen and managed at the paediatric surgery unit of a health centre in South West, Nigeria.

Study settings: The study was carried out in a tertiary hospital which serves as a referral centre from health institutions in Oyo North senatorial district of Oyo state, South West, Nigeria. The paediatric surgery unit of the health institution has two paediatric surgeons with a well-equipped facilities and other supportive medical staff (neonatologist, paediatrician, paediatric anaesthetist, radiologist) to take care of neonatal/children emergencies and elective cases.

The centre has a 22 bed paediatric ward, 10 bed neonatal ward and 6 bed neonatal intensive care unit. However, the centre lacked adequate facilities for paediatrics urological care such as neonatal/paediatrics renal replacement therapy other than peritoneal dialysis for patients with renal impairment; facilities for renal

radionuclide scan for differential analysis of renal function and obstruction in urinary tract; uroflowmeter, facilities for urodynamic studies and paediatric endo-urology.

In the period under review, the centre managed 145 paediatric surgical referrals from various health centres in the senatorial district.

Data collection: Information were obtained from the patients' case files retrieved from the hospital's medical records department. The information obtained included the age at presentation, clinical features and duration of observed symptoms, prenatal maternal ultrasonography, period of diagnosis of PUV(pre-natal or post-natal diagnosis), renal function assessment with serum electrolytes, urea and creatinine at the time of presentation, types of radiological diagnosis and features observed, initial medical treatment such as urethral catheterization, antimicrobial therapy and dialysis, definitive surgical procedures, post-surgical procedure urethral drainage and duration of drainage; the outcome of management of the patients; morbidity and mortality rate and duration of follow up of the patients.

Outcome of management was assessed by improvement in the obstructive symptoms, observed urine flow pattern with estimated urine flow rate (normal urine flow rate 15mls/sec), post procedural ultrasound to check for any improvement in the ultrasound features of hydronephrosis and analysis of post procedural changes in serum electrolytes, urea and creatinine.

Estimated urine flow pattern and flow rate were achieved by the physician visually observing the patients micturating after removal of urethral catheter with emphasis on the pattern of urine flow and an estimated flow rate derived by dividing amount of urine voided by time expended in voiding. In assessing the flow rate in neonates and infants, initiation of micturition was achieved by voiding- provocation manoeuvre in which the lower abdomen is lightly pressed with examiner's thumb; success of which depends on the neonate having significant urine in the urinary bladder during the manoeuvre. The urine voided was collected in a cellophane bag applied to the penis before voiding provocation manoeuvre and estimated urine flow rate gotten by dividing the voided volume by the micturition time.

Repeat valvotomy under general anaesthesia was done in any condition of failure of micturition with good flow rate after initial

valve ablation. Also, any case with suspected vesico-ureteric reflux (VUR) was referred to a health institution with more advanced facilities for further investigation and management.

Data analysis: Data collected were analyzed using the Statistical Package for the Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Categorical data were summarized as frequencies, proportions and rates, while continuous data were summarized using mean, standard deviation, median and range.

Ethical consideration: Ethical approval was obtained from the Ethical Review Committee of the health institution to carry out the retrospective review of cases of PUVs managed in the period under review.

RESULTS

Eight boys out of 145 paediatric surgical referrals had PUV and were managed in the period under review, accounting for 5.5% of all paediatric surgical referrals. The age at presentation ranged between the 1st day of life and 11 years, with a median age of 26 months. Three of the patients (37.5%) presented within the first year of life while the remaining patients presented after the first year of life [Table 1].

The most common presenting symptom in the patients was recurrent fever in six (75%) patients followed by four (50%) who had straining at micturition, and three (37.5%) had terminal dribbling of urine [Table 2]. Other symptoms included abdominal distension (37.5%), respiratory distress (25%), facial puffiness (25%) and feeling of incomplete bladder emptying (25%). Respiratory distress was observed only in the neonates.

Five (62.5%) of them had a palpable bladder at presentation. One of the patients had an associated unilateral inguinoscrotal hernia and another had an umbilical hernia. Five (62.5%) of the patients had laboratory evidence of urinary tract infection (UTI), and four (50%) presented in urosepsis, all requiring initial antimicrobial treatment. Three (37.5%) had evidence of renal insufficiency requiring initial peritoneal dialysis. The mean pre-operative serum creatinine was 4.7 (\pm 3.9) mg/dl (ref.: 0.1 to 1.2 mg/dl).

All the patients' mothers had antenatal ultrasound done, however, only one (12.5%) had a prenatal suspicion of bladder outlet obstruction made at 35 weeks of gestation. The remaining

seven patients (87.5%) were diagnosed in the post-natal period with abdominopelvic ultrasonography and expressed micturating cystourethrogram (MCUG) with findings of bilateral hydronephrosis, hydroureters, thickened bladder wall, dilated urinary bladder; and the "key-hole" sign on abdomino-pelvic ultrasonography and irregular bladder outline with dilated and elongated posterior urethra on MUCG.

All the patients had initial bladder drainage with Foley's urethral catheter appropriate size for age. Six of these patients (75%) had primary valve ablation with the Mohan's valvotome and thereafter, continuous bladder drainage was done using appropriate size of Foley's catheter for age. Mean duration of catheter drainage after valvotomy was 9 ± 3 days ($n=6$).

Five patients (83.3%) out of the 6 patients that had valve ablation with Mohan's valvotome showed immediate improvement in their obstructive urinary symptoms with an estimated urine flow rate of between 16 and 20mls/sec and improvement in the ultrasound features of bilateral hydronephrosis. In addition, five of the patients (83.3%) out of the 6 patients that had valve ablation with Mohan's valvotome had improved serum electrolytes, urea and creatinine after valve ablation with the Mohan's valvotome. The mean post-operative serum creatinine was 1.3 (\pm 0.7) mg/dl (ref.: 0.1 to 1.2 mg/dl).

A repeat valvotomy with Mohan's valvotome was done in one patient (16.7%, $n=6$) on account of persistent obstructive urinary symptoms. Following the repeat valvotomy, there was improvement in the obstructive symptoms but recurrent UTI persisted; thus, the possibility of an associated vesico-ureteric reflux (VUR) was considered. Hence, he was referred to a health institution with more advanced facilities for further investigation and management. Only two (33.3%) out of the 6 patients ($n=6$) who had valvotomy, had post- valvotomy UTI.

Three of the patients died, giving a mortality rate of 37.5% ; two patients died before valve ablation from overwhelming sepsis and renal failure while the third mortality was recorded in a patient who died a month after valve ablation from renal failure.

The median follow-up period after valve ablation was six months, with a maximum follow-up period of ten months. Renal function has remained within normal limits in these patients during the follow-up period.

DISCUSSION

Posterior urethral valves (PUV) have been described since the 18th century (3). They are the commonest congenital cause of bladder outlet obstruction in male children occurring in 1 in every 5,000 to 8,000 live male births (1,3,9). The exact aetiology of PUV is yet to be known (3). Posterior urethral valves result from an anterior insertion of the mesonephric ducts into the cloaca, leading to fusion of the ducts, which form abnormal ridges that become the valves (6). Progressive renal damage results from the back-pressure effect that occur due to bladder outlet obstruction. Twenty-five to 40% of patients with PUV eventually develop renal failure (10) and this complication can occur in spite of valve ablation (11).

A total of eight cases of PUV were managed within a 12-month period, accounting for five and a half per cent of all paediatric surgical referrals in the centre. This rate was similar to the average annual number of three to eight PUV cases reported by Uba et al, at Jos, North-Central Nigeria (9) and seven by Jaja et al, at Port Harcourt, South-South Nigeria (5). Higher incidences of PUV in Nigeria have been reported, thus highlighting the magnitude of this problem in a developing country (2,13,16).

Only three of the patients (37.5%) in this study presented within the first year of life, a finding similar to reports from Ibadan and Lagos, South west, Nigeria by Asinobi et al (17) and Ikuerowo et al (2). However, this was in contrast to 75.7% reported by Talabi et al from Ile-Ife, South-West Nigeria (12) and 68.3% by Uba et al from Jos, North-Central Nigeria (9). The median age at presentation was 26 months (2.2 years) with a range of one day to 11 years similar to the 2.5 years observed in the study by Okafor et al in Enugu (13).

The commonest symptoms observed was recurrent fever (75%) and straining at micturition (50%). This was similar to reports by Ikuerowo and Odetunde (2,7) but differs from most other studies where poor urinary stream was most common (1,9,11,13). Palpable bladder mass was the most common sign elicited among these patients (62.5%). Three (37.5%) presented with renal insufficiency, including one neonate, similar to the results from Ile-Ife and Enugu (7,12). In the study by Bhadoo et al, 42.8% (65 of 152) developed chronic renal failure (CRF) and they found no significant difference in the occurrence of CRF between those presenting before and after the first year of life (10). Peritoneal dialysis was used for renal

replacement therapy in the patients in this series, with satisfactory outcomes before proceeding to the surgical management.

The availability of prenatal ultrasonographic diagnosis of this condition has now made it possible for early detection and intervention. Suspicion of PUV can be made as early as 18 to 20 weeks gestation by maternal ultrasound scan showing oligohydramnios, bilateral hydronephrosis and a distended bladder (3,6). Fortunately, ultrasonography is readily available in most developing countries. However, prenatal diagnosis of PUV still remains low in Nigeria (2,12-14). In the present study, despite all the mothers having at least one antenatal ultrasound examination, only one (12.5%) had prenatal suspicion of PUV, and this was only made at 35 weeks gestation.

The mode of valve ablation in this study was valve ablation with Mohan's valvotome which has been shown to be effective method for valve ablation with comparable results to that achieved through endoscopy (16,18,19). This has proved to be valuable in our centre where facility for endoscopic ablation is unavailable. No mortality directly linked to the procedure was observed.

In this study, mortality rate was 37.5% which was higher than that observed in the other series earlier cited, of which 20% was the highest reported in Port Harcourt by Jaja et al (5). The higher mortality rate observed in this series may have been due to the small sample size and the delayed presentation in our patients.

Challenges in Management

Despite ultrasonography being readily available in Nigeria and antenatal maternal ultrasonography routinely done in the antenatal period as observed in this study, yet prenatal diagnosis of PUV is almost non-existent. Apparently, in most of the antenatal maternal ultrasound scan done emphasis was on the number of foetus, presentation and viability of the gestation with no prenatal screening for anomalies in the foetus.

Prenatal diagnosis of PUV allow for early intervention which may require in-utero ablation of the valve; however, such foetal intervention remain controversial. In addition, identification of patients that will benefit from it remain elusive; however, early delivery is still a viable option in fetuses with significant renal impairment (3,15). In developing countries, the opportunity to take such decision is often denied when prenatal diagnosis are not made.

In the absence of prenatal diagnosis, post-natal diagnosis and late presentation is the norm. The median age at presentation in this study was 26 months (2.2years). In respect to the late presentations, it is not unexpected to find substantial number of the patients with renal insufficiency (37.5%) at presentation that required peritoneal dialysis before the valve ablation.

Mohan's valvotomy have been found to be useful in valve ablation with comparable result with endoscopic valve ablation (16,18,19); Albeit, it may be associated with inadequacy of valve ablation (20) as the procedure is done blindly unlike endoscopic valve ablation which is usually performed under direct vision. In this study, there was failure of satisfactory ablation of valve in one of the patient which necessitated a repeat procedure. Although, no other morbidity or mortality was directly linked to the procedure; however, it should be emphasized that appropriate size of valvotomy should be used on the child's urethra as valvotomy larger than the urethra may result in urethral stricture (21).

Adequacy of valve ablation should result in improved urinary stream, objectively assessed by urinary flow rate. Urinary flow rate in an older child is usually assessed by uroflowmetry while in neonate, ultrasound flow probe can be used to assess urinary flow pattern as demonstrated by Olsen et al, in which an ultrasound flow probe connected to a flowmeter was mounted on the penis of the newborn to assess the flow curve configuration, maximum flow rate and voided volume (22). Such objective assessment of urinary flow rate was a challenge in our setting as visual assessment of the urine stream and subjective estimated flow rate were used to assess the patients' urinary stream in this study which is less than the ideal, due to non-availability of uroflowmeter and ultrasound flow probes in our institution.

CONCLUSION

A posterior urethral valve is a not an uncommon condition affecting young boys in our environment. It should be ruled out in boys with repeated presentation of fever or recurrent urinary tract infection. Parents may not be aware of obstructive urinary symptoms in their children; hence, physicians must have a high index of suspicion in diagnosing the condition in the post-natal period. Screening for foetal anomalies during routine antenatal maternal ultrasonography will ensure prenatal diagnosis of posterior urethral valve thereby reducing the

number of patients presenting late in our environment. Also, endoscopic valve ablation under direct vision may prevent inadequacy of valve ablation which may occur in blind valve ablation such as Mohan's valvotomy.

Conflicts of interest: The authors declare no conflicts of interest.

REFERENCES

1. Lukong CS, Ameh EA, Mshelbwala PM, Jabo BA, Gomna A, Anumah MA, et al. Role of vesicostomy in the management of posterior urethral valve in Sub-Saharan Africa. *J Pediatr Urol* 2014;10:62–66.
2. Ikurowo SO, Balogun BO, Akintomide TE, Ikurowo AOA, Akinola RA, Gbelee HO, et al. Clinical and radiological characteristics of Nigerian boys with posterior urethral valves. *Pediatr Surg Int* 2008;24:825. doi:10.1007/s00383-008-2163-3.
3. Nasir AA, Ameh EA, Abdur-Rahman LO, Adeniran JO, Abraham MK. Posterior urethral valve. *World J Pediatr* 2011;7:205–16.
4. Cuckow PM. Posterior Urethral Valves. In: Stringer MD, Oldham KT, Mouriquand PDE, editors. *Pediatr. Surg. Urol. Long-Term Outcomes*. 2nd ed, Cambridge: Cambridge University Press; 2006, p. 540–54.
5. Jaja T, Anochie IC, Eke FU. Posterior urethral valve in childhood in Port Harcourt, Nigeria. *PH Med J* 2012;6:10–6.
6. Elder JS, Shapiro E. Posterior Urethral Valves. In: Ashcraft KW, Holcomb GW, Murphy JP, Ostlie DJ, editors. *Ashcraft's Pediatr. Surg*. Sixth edition, London ; New York: Saunders/Elsevier; 2014, p. 762–72.
7. Odetunde OI, Odetunde OA, Ademuyiwa AO, Okafor HU, Ekwochi U, Azubuike JC, et al. Outcome of late presentation of posterior urethral valves in a resource-limited economy: challenges in management. *Int J Nephrol* 2012;2012. doi:10.1155/2012/345298.
8. Ansari MS, Singh P, Mandhani A, Dubey D, Srivastava A, Kapoor R, et al. Delayed Presentation in Posterior Urethral Valve: Long-Term Implications and Outcome. *Urology* 2008;71:230–4. doi:10.1016/j.urology.2007.09.037.
9. Uba AF, Chirdan LB, Ihezue CH, Ramyil VM, Dakum NK. Posterior urethral valves in childhood: Experience in a centre with scarce facilities. *Afr J Urol* 2007;13:124–131.
10. Bhadoo D, Bajpai M, Panda SS, others. Posterior urethral valve: Prognostic factors and renal outcome. *J Indian Assoc Pediatr Surg* 2014;19:133–7. doi:10.4103/0971-9261.136459.
11. Mirshemirani A, Khaleghnejad A, Rouzrokh M, Sadeghi A, Mohajerzadeh L, Sharifian M. Posterior urethral valves; a single center experience. *Iran J Pediatr* 2013;23:531–5.

12. Talabi AO, Sowande OA, Etonyeaku AC, Salako AA, Adejuyigbe O. Posterior urethral valves in children: Pattern of presentation and outcome of initial treatment in Ile-Ife, Nigeria. *Niger J Surg* 2015;21:151–156.
13. Okafor HU, Ekenze SO, Uwaezuoke SN. Posterior urethral valves: Determinants of outcome in a developing country. *J Paediatr Child Health* 2013;49:115–119.
14. Abiola B, Takure AO, Shittu OB, Okeke LI, Olapade-Olaopa EO. Review of posterior urethral valve in UCH Ibadan. *Afr J Urol* 2014;2:115.
15. Murphy JP, Gatti JM. Abnormalities of the Urethra, Penis and Scrotum. In: Coran AG, Adzick NS, editors. *Pediatr. Surg. Full Access More Expert.*, vol. 2. 7th ed, Philadelphia, Pa: Elsevier Mosby; 2012, p. 1555–63.
16. Ikuerowo SO, Omisanjo OA, Balogun BO, Akinola RA, Alagbe-Briggs OT, Esho JO. Mohan's valvotome for the ablation of posterior urethral valves. *J Pediatr Urol* 2009;5:279–282.
17. Asinobi AO, Gbadegesin RA, Shittu OB. A review of cases of posterior urethral valves seen at the University College Hospital, Ibadan (Nigeria). *Pediatr Medica E Chir Med Surg Pediatr* 2003;26:430–433.
18. Sudarsanan B, Nasir AA, Puzhankara R, Kedari PM, Unnithan GR, Damiseti KRP. Posterior urethral valves: a single center experience over 7 years. *Pediatr Surg Int* 2009;25:283–7. doi:10.1007/s00383-009-2332-z.
19. Abraham MK, Prashanth, Bindu S, Ramakrishnan P. Valvotome-Revisited. *J Indian Assoc Pediatr Surg* 2007;12:185–6
20. Shittu OB, Asinobi AO. Long-term outcome of posterior urethral valves ablation using Mohan's urethral valvotome. *West Afr J Med.* 2004; 23:35-7.
21. Mohan KA. Mohan's Urethral valvotome: A new instrument. *J Urol.*1990; 144:1196-1198.
22. Olsen LH, Grothe I, Rawashdeh YF, Jørgensen TM. Urinary flow patterns of healthy newborn males. *J Urol.*2009;181(4):1857-61

Table 1: Frequency distribution of age at presentation and mortality

Age at presentation	n (%)	Mortality (%)
< 1year	3(37.5)	2(25.0)
>1year	5(62.5)	1(12.5)
Total	8(100)	3 (37.5)

Table 2: Distribution of clinical features at presentation

Clinical features	Frequency (%) (n=8)
Recurrent fever	6 (75)
Palpable bladder	5 (62.5)
Urinary tract infection	5 (62.5)
Straining at micturition	4 (50)
Poor urine stream	4 (50)
Urosepsis	4 (50)
Abdominal distension	3 (37.5)
Terminal dribbling	3 (37.5)
Renal failure	3 (37.5)
Facial swelling	2 (25)
Incomplete bladder emptying	2 (25)
Respiratory distress	2 (25)
Prenatal diagnosis	1 (12.5)