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### Pediatric Urology

Original article

# Are early prognostic indicators reliable in posterior urethral valves management?

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#### KEYWORDS

PUV;  
ESRD;  
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Creatinine at diagnosis

#### Abstract

**Objective:** To identify indicators that predict outcome in posterior urethral obstruction management in a resource-constrained environment with emphasis on the importance of early indicators.

**Subjects and methods:** A retrospective review of all children who were managed for posterior urethral obstruction from 2002 to 2012 was done. Variables studied were: age at diagnosis (AgD) and of ablation, creatinine at diagnosis (CrD), nadir creatinine (CrN), vesicoureteric reflux (VUR), urinary diversion, and urodynamic study (UDS) findings. These were evaluated against two groups of patients—those with end stage renal disease (ESRD)-Group A and those with normal renal function-Group B. Significant variables were entered into a multivariate logistic regression to identify the independent prognostic factors that determine progression to ESRD. The independent factors were further analyzed with the receiver operating characteristics (ROC) to identify cutoff levels. The data is expressed as mean  $\pm$  SD and median (IQR). A p-value of 0.05 was regarded as significant.

**Results:** Sixty patients had adequate documents for evaluation. ESRD was identified in 30% of the cases. The AgD was 2.5 weeks (1–18 weeks). CrD, CrN, abnormal UDS, and VUR were significant prognostic indicators of ESRD ( $p=0.0001$ ), with CrN and CrD being independent factors on regression analysis. CrD value of  $\geq 102 \mu\text{mol/L}$  had sensitivity of 94.4% and specificity of 68.3%, with a PPV of 56.7%

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(CI: 37.4–74.5) and a NPV of 96.6% (CI: 82.2–99.9). CrN of  $\geq 89 \mu\text{mol/L}$  had sensitivity of 27.8% and a specificity of 95.1% with a PPV of 71.4% (CI: 29%–96.3%) and NPV of 75% (CI: 61.1%–86%) in predicting ESRD.

**Conclusion:** In our environment, a child with initial creatinine value of less than  $102 \mu\text{mol/L}$  may be classified as unlikely to develop ESRD. Additionally, a nadir creatinine greater than  $89 \mu\text{mol/L}$  may increase the probability of developing ESRD. While nadir creatinine has consistently been identified as independent indicator of outcome, its value is evaluated after a year of management; however, early indicator like creatinine at diagnosis may provide essential monitoring information at the onset of treatment.

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## Introduction

Obstructive uropathy is second to dysplastic kidneys as the most common primary diagnosis of recipients of renal transplantation in pediatric population, according to the North American Pediatric Renal Trials and Collaborative Studies 2010 report [1]. Posterior urethral obstruction is the commonest cause of obstructive uropathy in children, pathology that is now being recognized as a Congenital Obstructive Posterior Urethral Membrane (COPUM) [2–4]. However, despite several attempts to introduce this new term, Hugh Young's classification remain the accepted nomenclature [5]. Creatinine has long been identified as an early prognostic indicator of children with posterior urethral valves [6], and creatinine value measured after bladder decompression has been found to correlate significantly with the development of end stage renal disease later in life. Nadir creatinine is the most consistent prognostic factor identified in PUV management outcome [7–9]. Other factors such as vesicoureteral reflux (VUR), a pop off mechanism, late presentation, prenatal diagnosis, echogenic kidneys etc. have not consistently been identified in recent studies [7,8].

The majority of research into PUV comes from the developed world. With the need of renal transplantation increasing in South Africa, coupled with the limited resources at our disposal, knowing which prognostic factors determine outcome in the management of PUV will not only help identify patients who need increased monitoring, but also reduce the effect of increasing medical cost on the population and provide background for parental counseling. Regular monitoring may also prevent or delay the progression of valve children to end stage renal disease (ESRD). In this regard, the role of early prognostic indicators cannot be overemphasized, as they may enhance the efficient application of health care resources. This is a single center study aimed at identifying the prognostic factors that may determine the outcome of PUV management.

## Subjects and methods

After institutional review board approval (HREC REF: 257/2015), the medical records of boys managed for posterior urethral obstruction in Red Cross War Memorial Children's Hospital from 2002 to 2012 were identified. Included patients had at least two years of follow up; those lost to follow up, with insufficient data, and loss of records/missing data were excluded. Data was collected using

Excel spreadsheet (Microsoft Excel, 2010 Microsoft Corporation) and analyzed using Stata (Stata/IC 13.1, 1985–2013 StataCorp LP).

PUV diagnosis is made using patients' history, physical examination, voiding cystourethrogram (VCUG) findings, and further confirmed during cystoscopy for valve fulguration. We identified those with moderate to severe renal impairments (chronic kidney disease stage 3b and above i.e. glomerular filtration rate (GFR) less than  $60 \text{ ml/min/1.73 m}^2$ ) as Group A. While those with normal to mild renal impairment ( $\text{eGFR} > 60 \text{ ml/min/1.73 m}^2$ ) were identified as Group B. GFR was measured with the modified Schwartz formula. Chronic kidney disease (CKD) refers to a state of irreversible kidney damage and/or reduction of kidney function, which can be progressive. Subsequently, these 2 groups were evaluated against the following prognostic indicators: serum creatinine at diagnosis (CrD)—serum creatinine value recorded when the patient is first seen, nadir creatinine (CrN)—defined as the lowest serum creatinine in the first year of life, VUR, urinary diversion, bladder neck incision (BNI), and urodynamic study (UDS) findings. Data was also collected on the age of diagnosis (AgD), age at ablation (AgS), and if there was antenatal diagnosis. Means were taken for normally distributed variables and median for non-normally distributed ones. Comparisons were determined and tested using Fisher Exact test. The significant factors were further evaluated with multivariate logistic regression to identify the independent determinants of progression to significant renal impairment. The independent factors were further analyzed to identify cutoff levels that can enhance patients' selection for more aggressive monitoring. The receiver operating characteristics (ROC) curve was used to estimate the accuracy of cutoff levels to distinguish the two groups. The data is expressed as mean  $\pm$ SD and median (IQR). A p-value of 0.05 was regarded as significant.

## Results

In all 75 folders were accessed, 15 eliminated because of insufficient data and/or lost to follow-up, leaving 60 for analysis. The mean age at diagnosis was 2.5 weeks (IQR 1–18) (Group A: 2 weeks, Group B: 3 weeks,  $p=0.9$ ). Antenatal diagnosis was made in only 25% of the patients. And, 30% (18/60) of the study population developed significant renal impairments over a mean follow-up of  $7.8 \pm 4.90$  years. The follow-up of Group A was  $9.4 \pm 5.89$  years and that of Group B,  $7.4 \pm 4.14$  years ( $p=0.18$ ). Serum creatinine at diagnosis, nadir creatinine, abnormal urodynamic value, and vesicoureteral reflux were

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