



# Risk factors for postobstructive diuresis in pediatric patients with ureteropelvic junction obstruction, following open pyeloplasty in three high complexity institutions

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## Keywords

Hydronephrosis; Ureteric obstruction; Polyuria; Risk factors; Diuresis

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## Summary

### Introduction

Postobstructive diuresis (POD) is a polyuric state in which large quantities of salt and water are eliminated after solving a urinary tract obstruction. These patients are at increased risk of severe dehydration, electrolytic disturbances, hypovolemic shock, and death. Ureteropelvic junction obstruction (UPJO) is the most common etiology of collecting system dilatation in the fetal kidney, and a significant number of patients require pyeloplasty. There are limited data regarding prognostic risk factors for POD in this scenario.

### Objective

To describe possible clinical risk factors for POD in the pediatric population after open pyeloplasty.

### Study design

This was a retrospective case series study of consecutive patients diagnosed with UPJO at three high complexity centers, managed with open pyeloplasty from 2006 to 2016. Multiple qualitative and

quantitative variables possibly associated with POD were included according to the literature review. They were statistically analyzed with STATA 14 software.

### Results

A total of 88 patients with UPJO following open pyeloplasty were analyzed. Twenty-seven patients (30%) had POD. A tendency to present POD in younger patients was found, with a mean age of 20.2 months vs. 72.3 months. There was also an increased risk of POD in patients with previous diagnosis of tubular acidosis.

### Conclusions

There are no data about prognostic clinical risk factors for POD after open pyeloplasty in the pediatric population. Our study corresponds to one of the larger series reported so far. It suggests that younger patients and patients with a previous diagnosis of tubular acidosis could be at greater risk of POD. Consequently, prospective studies are required for validation of our results, and possible impact on patient follow-up.

**Summary table.** Risk factors for POD: results of the univariate analysis with statistical significance.

Variable	Patients with no POD <i>n</i> = 61	Patients with POD <i>n</i> = 27	<i>p</i>
Median (range) age, months	72.3 (1–192)	20.2 (2–120)	0.005
Previous tubular acidosis, <i>n</i> (%)	1 (2)	3 (11)	0.049

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## Introduction

Postobstructive diuresis (POD) is a polyuric state in which large quantities of salt and water are eliminated after the relief of a urinary tract obstruction [1]. The incidence of POD across the studies varies between 0.5% and 52% [2]. In the pediatric population, when there is a urinary output (UO) greater than 5 cc per hour for 2 consecutive hours, it is considered to be compatible with POD. These patients have an increased risk of severe dehydration, electrolytic disturbances, hypovolemic shock, and death if proper management is not started [1]. Consequently, POD requires strict monitoring, in addition to electrolytes and intravenous fluid reposition. UO should be registered every 2 h, and vital signs every 6–8 h. Additionally, serum levels of potassium, magnesium, phosphate, urea, and creatinine should be measured every 12–14 h [3].

It is known that ureteropelvic junction obstruction (UPJO) is the most common etiology of significant collecting system dilatation in the fetal kidney [4], and depending on the severity of the obstruction, about 35% will undergo surgery [5,6]. However, there are no literature data regarding clinical prognostic risk factors for POD after open pyeloplasty. Given the potential lethal consequences of this pathologic state, we aimed to describe clinical risk factors for POD in the pediatric population in this setting. Our hypothesis was that younger patients and those with more severe upper tract dilation could have higher risk of POD after pyeloplasty.

## Materials and methods

We conducted a retrospective case series study of consecutive patients diagnosed with UPJO, admitted during the period of 2006–2016, at three high complexity centers. They were managed with open pyeloplasty performed by the same pediatric urologist.

Indications for surgical intervention included: 1) presence of symptoms associated with the obstruction (i.e. pain, urinary tract infections, stones, failure to thrive, abscess, HTN, or sepsis), and 3) differential renal function <40% with impaired drainage (as indicated by T1/2 > 20 min), or worsening renal function by dynamic renal scintigraphy [7,8].

The diagnosis of POD was based on the following definition: urinary output greater than 5 cc per hour in 2 consecutive hours.

As a protocol in our institutions, all patients are stented during surgery and the double J stent is retained for 6 weeks.

Treatment of POD after open pyeloplasty in these centers included monitoring of: 1) vital signs and diuresis every hour, 2) serum electrolytes, serum urea nitrogen, creatinine, and fluid balance twice a day, and 3) weight daily. If POD occurred, urinary losses were compensated with intravenous fluids. Considering UO, bladder catheters were retained in all patients with POD until resolution and discharge, usually during 72 h.

The following data were collected from medical and nurse charts: 1) general demographic characteristics, 2) obstruction laterality, 3) antero-posterior diameter (APD)

of the renal pelvis (prenatal and pre-surgical), 4) comorbidities (HTN, renal tubular acidosis), 5) preoperative glomerular filtration rate (GFR) estimated by diuretic renogram, 6) preoperative DMSA uptake of the involved kidney, 7) intravenous fluids used trans operative, and 8) pre-surgical use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium antagonists, or diuretics. Outcomes after the release of obstruction were evaluated taking into account: electrolytes, serum creatinine, and urea levels as well as UO during the first 3 days following surgery.

Data are presented as percentage or median (range) values. Risk factors for POD occurrence were identified with univariate analysis using non-parametric tests. The statistical analysis was performed using the STATA 14 statistical software. A *p* value < 0.05 was considered to indicate statistical significance.

## Results

During the study period, 96 patients underwent pyeloplasty for UPJO at three high complexity centers. It was only possible to analyze 92% of these cases, because of a lack of information for eight patients. POD occurred in 27 (30%) patients during the first 72 postoperative hours, with a mean duration of 39.7 h.

In terms of laterality, there was a left predominance in patients with POD; while in patients that did not present with POD, UPJO was more common on the right side.

The majority of patients had no comorbidities: 91.8% in the group with no POD, and 81.4% in the POD group. Nonetheless, comorbidities found were hypertension, renal tubular acidosis, asthma, duplex collecting system, and renal hypoplasia. The renal hypoplasia was mild and present in only one patient, who did not have POD.

Unfortunately, we had a significant amount of non-registered data. About 30% of information on electrolyte levels was missing, as well as information on preoperative estimated renal function. We also had a 15% rate of absent numbers regarding the APD of the renal pelvis.

Finally, changes in serum sodium, potassium, creatinine, and urea were not statistically different whether POD occurred or not. Moreover, we did not find any difference between both groups in terms of renogram eGFR or DMSA uptake of the involved kidney.

The univariate analysis of possible risk factors for POD is shown in Table 1. There was a tendency to POD in younger patients - mean age of 20.2 months vs. 72.3 months. There was also an increased risk of POD in patients with previous diagnosis of tubular acidosis.

A multivariate regression was performed to predict the value of POD based on age, weight, and previous tubular acidosis. These variables statistically significantly predicted POD and are shown in Table 2.

## Discussion

There are limited literature data about prognostic risk factors for POD following pyeloplasty in children. Nevertheless, it is a prevalent entity (30% in our cohort) that

can compromise the patient's life and requires early management.

An effort has been made to describe prognostic factors for POD. Hamdi and colleagues [9] studied adult patients with post renal acute renal lesion. They found high serum bicarbonate and high creatinine levels together with urinary retention as independent predicting factors for POD. Furthermore, some studies have suggested the presence of renal failure, heart failure, volume overload, and nervous central system depression as risk factors for POD [3]. However, these parameters have not been described in the pediatric population.

According to *in vitro* studies, there is a decrease in water and sodium reabsorption in the proximal tubule, distal tubule, and collecting system after pyeloplasty, which is generally linked with aquaporins (AQ) decreased in the collecting system [10]. Based on these data, Li and colleagues [11] evaluated 22 pediatric patients with unilateral UPJO. They found an association of polyuria with down-regulation of urinary exosomal AQP1 in the post-obstructive kidney, as well as an increase in the transforming growth factor  $\beta$ 1 (TGF- $\beta$ 1). These biomarkers require further research and validation.

Similarly, Jensen and colleagues [10] studied changes in water channels after the resolution of bilateral ureteral obstruction in mice. They described a decrease in the expression of AQP1, AQP2, and AQP3. They also found that AT1 antagonist (candesartan) attenuated the decrease in GFR, urinary production, and suppression of AQP, as well as the induction of COX-2 in the inner medulla. These findings suggest that angiotensin II influences directly and indirectly the production of POD [10]. In our case series none of the patients managed with ARBs and ACE inhibitors presented with POD. However, we were not able to demonstrate a protective role of these drugs because of the small sample of patients using them.

**Table 2** Risk factors for POD after open pyeloplasty: results of the multivariate analysis.

Independent variables	OR	<i>p</i> value	95% CI
Age	0.97	0.004	0.951–0.990
Weight	0.67	0.021	0.567–0.954
Previous tubular acidosis	3.54	0.024	1.117–10.63

Urinary flow obstruction gives place to a series of renal changes. The magnitude depends on the life stage in which it is established, and the type of blockage produced. It has been demonstrated that significant urinary obstruction in an early stage of gestation, causes alterations in renal growth and maturation. This is supported by a decrease in the DNA renal content and number of nephrons, as well as vascular, glomerular, tubular, and interstitial immaturity [12]. Our study supports the hypothesis that younger patients are at greater risk of POD. Taking into account the aforementioned data, it may be inferred that these patients have a deeper depression of AQ expression, and therefore a more severely impaired urine-concentrating capability that predisposes them to an important imbalance of water and electrolyte metabolism.

In spite of the evidence of functional tubular damage, decreased sodium reabsorption, and activation of natriuretic factors after releasing a obstruction [13], post-operative electrolytes values were not associated with an increased risk of POD in this cohort. This may be the result of an important amount of missing data in our charts.

On the other hand, we expected to show a greater rate of POD in patients with more severe urinary tract dilatations. However, severity is not only determined by the anteroposterior diameter of the renal pelvis, but also by

**Table 1** Risk factors for POD after open pyeloplasty: results of the univariate analysis.

Variable	Patients with no POD	Patients with POD	<i>p</i>
	<i>n</i> = 61	<i>n</i> = 27	
Median (range) age, months	72.3 (1–192)	20.2 (2–120)	0.0053
Male gender, <i>n</i> (%)	47 (77)	19 (70)	0.505
Left side UPJO, <i>n</i> (5)	23 (38)	17 (62)	0.028
Median (range) weight, kg	22.6 (4–60)	9.5 (3.7–29)	0.0009
Median (range) value of mean APD preoperatively, mm	34.8 (7–93)	28.3 (11–60)	0.519
Median (range) value of mean prenatal APD, mm	17.1 (8–36)	21 (6.3–44)	0.892
Median (range) urinary output (mL/kg/hour)	3.1 (0.5–4.6)	8.2 (5–15)	
Median (range) previous GFR, mL/min/m <sup>2</sup>	97.4 (49–153)	93.3 (43.8–149)	0.285
Median (range) DMSA uptake of the involved kidney, %	46.8 (17–100)	55.4 (33–100)	0.265
Median (range) serum urea, mg/dL	8.6 (2.9–15)	12.5 (3.4–27)	0.317
Median (range) serum K <sup>+</sup> mEq/L	4.5 (3.8–5.2)	4.4 (3.6–5.4)	0.654
Median (range) serum sodium, mEq/L	138.6 (131–148)	139.2 (136–143)	0.654
Median (range) serum Cr, mg/dL	0.5 (0.1–1.1)	0.4 (0.1–1.2)	0.465
Previous hypertension, <i>n</i> (%)	4 (7)	1 (4)	0.594
Previous tubular acidosis, <i>n</i> (%)	1 (2)	3 (11)	0.049
Previous treatment with ACE inhibitors, <i>n</i> (%)	2 (3)	0	0.341
Previous treatment with calcium antagonists, <i>n</i> (%)	2 (3)	0	0.341
Previous treatment with diuretics, <i>n</i> (%)	0	3 (11)	0.008

the presence of calix dilatation, thickness and echogenicity of the renal parenchyma. This corresponds to a bias in our study, because it was not possible to evaluate the ultrasound images in most of the patients, and there were no specific data regarding the above mentioned parameters in our clinical charts.

Patients with obstructive uropathy may present a syndrome of hyperkalemic distal renal tubular acidosis. In some patients, this syndrome results from a defect in hydrogen and potassium secretion in the distal nephron rather than from aldosterone deficiency [14]. However, a resistance to the action of parathyroid hormone and aldosterone has also been demonstrated [12]. These data agree with our findings of a possible association of POD with previous renal tubular acidosis.

Limitations of the present study should be underlined. The sample size was small, and the correlation of some variables may have reached statistical significance if more patients had been included. Additionally, because of its retrospective design, important data were missing, which limited analysis and its statistical validity. Our results must be interpreted carefully.

In conclusion, there is limited evidence in the literature about prognostic clinical risk factors for POD after open pyeloplasty in the pediatric population. Our study corresponds to one of the larger series reported so far. It suggests that patients of younger age and those with a previous diagnosis of tubular acidosis could be at greater risk for presenting POD as a complication. Consequently, prospective studies are still required for validation of our results, and their possible impact in patient follow-up.

### Conflict of interest

None.

### Funding

None.

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