

Research Article

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# Assessment of Prognostic Factors in Children with Renal Tubular Acidosis Type IV Overwhelmed by Bilateral Obstructive Uropathy

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**Introduction:** Hyperkalemia renal tubular acidosis (type IV) occurs secondary to impaired renal responsiveness to aldosterone. This can occur chronically in infants and children with a history of obstructive uropathy. The aim of this study was to assess of prognostic factors in children RTA type IV overwhelmed by bilateral obstructive uropathy.

**Materials and Methods:** In this study, we recruited and observed 48 male patients with both bilateral obstructive uropathy at the urinary bladder outlet and RTA type IV for two years. In this period, we registered patients' demographic data; also, children's growth, sonographic data, renal function tests and serum electrolytes underwent serial assessment and in if clinically indicated, the patients were treated with drugs like citrate sodium and Kay oxalate.

**Results:** Frequent urinary tract infection (p=0.0011), abnormal <20 weeks gestation sonography results like bilateral hydronephrosis (p=0.00001), birth weight below 2500 gr (LBW) (p=0.0014), preterm delivery (p=0.001), maternal age at birth below 20 years (p=0.0018), pregnancy more than 2 times (p=0.004), admission due to respiratory problems during infancy (p=0.003) and gestational diabetes (P=0.001) were significantly associated with a poor prognosis.

**Conclusions:** Considering the results of this study, it seems logical to consider abortion in case of renal hydronephrosis and dysplasia in gestational age below 20 weeks.

**Keywords:** Hyperkalemia; Urologic Diseases; Renal Tubular Acidosis

**Running Title:** Prognostic Factors in RTA Type IV

## Introduction

Type IV renal tubular acidosis (RTA) occurs secondary to impaired renal responsiveness to Aldosterone (pseudohypoaldosteronism). Acidosis is the inevitable result since Aldosterone has a direct effect on H<sup>+</sup>/ATPase responsible for hydrogen secretion [1]. Moreover, Aldosterone is a potent stimulant for potassium secretion in the collecting tubule; therefore, lack of Aldosterone

results in hyperkalemia in children. Aldosterone unresponsiveness is usually a common cause of type IV RTA. This can occur transiently, during an episode of acute pyelonephritis or acute urinary obstruction in children. It may occur chronically, particularly in infants and children with a history of obstructive uropathy [2]. The latter patients can have significant hyperkalemia, even in instances when renal function is normal or only mildly

impaired [3]. Patients with type IV RTA, like those with type I and II RTA, can present with growth failure in the first few years of life. Polyuria and dehydration (from salt wasting) are common [3]. Rarely, patients (especially those with pseudohypoaldosteronism type 1) present with life-threatening hyperkalemia. Patients with obstructive uropathy can present acutely with signs and symptoms of pyelonephritis, such as fever, vomiting, and foul-smelling urine [3]. Urinary tract obstruction can result from congenital (anatomic) lesions or can be caused by trauma, neoplasia, calculi, inflammatory processes, or surgical procedures although most childhood obstructive lesions are congenital [2]. Obstructive lesions occur at any level from the urethral meatus to the calyceal infundibulum. The pathophysiologic effects of obstruction depend on its level, the extent of involvement, the child's age at onset, and whether it is acute or chronic [2]. Obstruction of the urinary tract generally causes hydronephrosis, which is typically asymptomatic in its early phases. An obstructed kidney secondary to a ureteropelvic junction (UPJ) or ureterovesical junction obstruction can manifest as a mass or cause upper abdominal or flank pain on the affected side [2]. Pyelonephritis can occur because of urinary stasis. An upper urinary tract stone can occur, causing abdominal and flank pain and hematuria. With bladder outlet obstruction, the urinary stream may be weak; urinary tract infection is also common. Many of these lesions are identified by antenatal ultrasonography; an abnormality involving the genitourinary tract is suspected in as many as 1/100 fetuses [2]. In our study, we focused on the assessment of prognostic factors in children RTA type IV overwhelmed by bilateral obstructive uropathy.

### Materials and Methods

In this study, we recruited and observed 48 male patients with obstructive uropathy and a diagnosis of RTA type IV at birth or during infantile period who had hydronephrosis, dysplasia, hydrouretronephrosis or urinary bladder dilation in fetal sonography. The patients were observed for two years. We registered patients' demographic data about birth weight, term situation at birth, maternal age at birth, gestational diabetes, number of pregnancies, admission due to respiratory problems during infancy, and the results of paraclinical tests like serum urea, creatinine, sodium, potassium, bicarbonate, urine analysis and culture and serial

sonography (for kidney growth). Poor prognosis was suggested if three or more of the following criteria were observed simultaneously:

1. GFR (Glomerular filtration rate) modifications
2. Impairment of growth and development
3. DMSA (dimercaptosuccinic acid) scan modifications
4. DTPA (Diethylene Triamine Pentacetic Acid) scan modifications
5. Continued electrolyte abnormalities (hyperkalemia, acidosis)
6. Death

Cases with a need for surgery were referred. Upon clinical indication, prophylactic antibiotics with 1/3 of the therapeutic dose, citrate sodium, and Kay oxalate were administered. In this period, the child's growth, height, weight, head circumference and development were observed. The data was analyzed with SSPS version PASW statistics 18 (SPSS Inc., Chicago, IL, USA) using odds ratio, chi square and logistic regression test.

### Results

Of 48 children in our study, 39 (81.25%) had the criteria of poor prognosis. The majority of the children had a history of admission due to respiratory problems during infancy. As a result, a significant relationship was found between admission due to respiratory problems during infancy and poor prognosis ( $P=0.003$ ). Our 2-year study showed that of 48 children, 37 (77.08%) had a history of frequent UTI; these children also had the criteria of poor prognosis ( $P=0.0011$ ). Regarding gestational diabetes, our results showed that of 39 children with poor prognosis, 33 (84.6%) had a history of gestational diabetes; therefore, this variable had a significant relationship with poor prognosis in our study population ( $P=0.001$ ). Moreover, the results showed that birth weight below 2500 gr (LBW) ( $p=0.0014$ ), infants and children with abnormal <20 weeks gestation sonography results like bilateral hydronephrosis ( $p=0.00001$ ), preterm delivery ( $p=0.001$ ), maternal age at birth below 20 years ( $p=0.0018$ ) and pregnancy more than 2 times ( $p=0.004$ ) were significantly associated with poor prognosis criteria. (Table 1)

**Table 1.** Correlation between demographic data and poor prognosis criteria in patients

|                                | Definition     | Number of patients | Number of Poor prognosis patients | Statistical test PV |
|--------------------------------|----------------|--------------------|-----------------------------------|---------------------|
| <b>Birth weight</b>            | VLBW           | 4                  | 0 (0%)                            | 0.0014              |
|                                | LBW            | 20                 | 19 (95%)                          |                     |
|                                | NL             | 21                 | 2 (9.5%)                          |                     |
|                                | >4000 g        | 3                  | 0 (0%)                            |                     |
|                                | total          | 48 (100%)          | 21 (43.7%)                        |                     |
| <b>Term situation at birth</b> | Term: 37-40 w  | 29                 | 2 (6.8%)                          | 0.001               |
|                                | Pre term <37 w | 19                 | 16 (84.2%)                        |                     |
|                                | Post term>40w  | 0                  | 0 (0%)                            |                     |
|                                | total          | 48 (100%)          | 18 (37.5%)                        |                     |
| <b>Mother's age at birth</b>   | <20 years      | 19                 | 18 (94.7%)                        | 0.0018              |
|                                | 20-30 years    | 24                 | 3 (12.5%)                         |                     |
|                                | >30 years      | 5                  | 0 (0%)                            |                     |
|                                | total          | 48 (100%)          | 21 (43.7%)                        |                     |
| <b>Number of pregnancy</b>     | 1 time         | 13                 | 0 (0%)                            | 0.004               |
|                                | 2 times        | 21                 | 2 (9.5%)                          |                     |
|                                | >2 times       | 14                 | 13 (92.8%)                        |                     |
|                                | total          | 48 (100%)          | 15 (31.2%)                        |                     |

Key: VLBW= Very Low Birth Weight (<1500 g.), LBW= Low Birth Weight (1500-2500 g.), NL: Normal (2500-4000 g.) w= week, PV= P. value<0.05 is considered as the level of statistical significance.

### Discussion

Considering the results of this study, it seems logical to consider abortion in case of renal hydronephrosis and dysplasia in gestational age below 20 weeks. Moreover, medical care during pregnancy for a safe and term delivery with suitable fetus weight can considerably eliminate gestational complications and hypoxia seen in pre-term deliveries and low birth weight infants. On the other hand, since conception before 20 years of age is more likely to result in pre-term delivery, we recommend postponing conception to after this age to reduce pre-term delivery related complications. Studies dealing with obstructive uropathy have not cited RTA IV related complications. Nevertheless, in a study by Rothstein M [4], RTA IV was found to be more common in patients with urinary outlet obstruction than other causes of bilateral obstruction. In other study performed by Kuymars [5], obstructive uropathy with low volume of amniotic fluid was associated with poor prognosis. In a study conducted by Gargah T [6], children with PUV obstruction who had renal dysplasia renal scar in fetus or infantile period had worse outcomes. Nasir AA [7], similar to us, concluded that dysplasia before 20 weeks gestation and persistence of serum creatinine above 0.8

heralded poor prognosis. Narasimhaakl [8] did not report any favorable prognostic factor. Similar to our findings, a study by Becher A [9] showed that sonography problems before 20 weeks gestation were associated with a poor prognosis. In another study by Salam MA [10], surgical intervention during pregnancy to reduce the pressure on renal parenchyma showed better results than non-surgical methods.

### Conclusions

None of these studies focused on RTA type IV; therefore, it is prudent to lunch similar studies with more patients in different centers and longer observation periods to assess the overall prognosis in such patients.

### Conflict of Interest

None declared

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None declared

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