# Patterns of renal tubular disorders in Egyptian children: a single center study

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# Patterns of renal tubular disorders in Egyptian children: a single center study

Thesis

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## Introduction

Fluids, electrolytes, and acid-base regulations are the main functions of renal tubules(1). Defects of these functions give rise to several disorders(2). In Egypt, little data is available. Many of these cases are diagnosed late, therefore Early suspicion for diagnosis can improve the overall clinical outcome of these children. Starting management early will help those children have a better life. Therefore, awareness about these disorders and long-term outcome is important(3). We present the clinical characterizations of many tubular disorders and the follow up in our center with emphasis on growth and renal functions outcomes.

## Aim of the work

The aim of this study is to reveal the different clinical presentations and the main lab features of renal tubular disorders in children to promote early recognition and management in addition to monitoring growth and glomerular filtration rate.

## Patients and methods

**-Place of the study:**

Sohag University Hospital, Pediatric Department, Nephrology Unit.

**-Type of the study:** Retrospective and prospective study.

-**Study period:** 6-12 months after protocol acceptance.

**-Patients: -**

This study will include all children who have renal tubular disorders (inpatient and outpatient) in the Pediatric Department, Sohag University Hospital.

**- Inclusion criteria: -**

All children aged from one month to 18 years who have renal tubular disorders.

**Exclusion criteria:**

Children who have renal tubular disorders secondary to drugs, intoxication, obstructive uropathy or transient in nature.

**-Methods:**

Records of all children who have renal tubular disorders in the nephrology center from 2015 to 2020 and the children following up from April 2021 to December 2021 will be subjected to:

1-History taking with emphasis on age, age at diagnosis, sex, family history, Failure to thrive, polyuria, polydipsia, consanguinity, dehydration episodes, lack of appetite, vomiting, seizures, weakness, photophobia, and deafness.

2-Complete physical examination with emphasis on general condition, signs of rickets, polyuria (>4 ml/kg/hour), bone deformities and developmental milestones.

3-Growth assessment was done by recording height and weight according to the WHO growth charts and z scores. (Failure to thrive means weight and height below the 3$^{rd}$ centiles).

4-Investigations done for children included:

a- Blood gases and anion gap estimation

b- Electrolytes: serum sodium, potassium, calcium, chloride, and phosphorus

c- Urine analysis and urinary calcium creatinine ratio

d- Estimation of GFR

e- Renal ultrasound

f- Complete blood count

g- Others may be needed e.g., bone radiograph, serum magnesium, and urinary chloride.

Metabolic acidosis means decreased serum HCO3 concentration and pH below 7.35.

Metabolic alkalosis means elevated serum HCO3 concentration and pH above 7.45.

The glomerular function was assessed by estimated glomerular filtration rate (eGFR) calculated using Schwartz formula.[5]

**Statistical analysis:**

We expressed the data as percentage, median with range. Data was analyzed using Wilcoxon test to compare the diverse groups of renal tubular disorder. Qualitative data was presented as number and percentage and compared using Chi square test. P value < 0.05 was considered significant. Serial weight and height were measured and z scores and percentiles were calculated. GFR was estimated and monitored using Schwartz formula(4).

**-Ethical consideration: -**

The protocol will be submitted to Medical Research Ethical Committee for approval.

Written informed consent will be taken from all participating patients or their families.

## Results:

58 children with renal tubular disorders were candidates. Duration of follow up ranges from (6-132) month with median 12 month. In our study, there were 33 males and 25 females.

# Patterns of renal tubular disorders:

Various renal tubular disorders were noticed. DRTA and Barter S were the most common encountered tubulopathies.

# Diagnosis:

The median age at diagnosis was 17 month (ranges from 3-84 month). The age at diagnosis was less or equal 12 month in 44.83% of cases, (13-36) months in 36.21%, (37-72) month in 15.52% and 73 month or more in 3.45%. Clinical manifestations were present several months prior to definitive diagnosis was made.

Table: patterns of encountered renal tubular disorders

| Renal tubular disorder | Total number<br><br>N= 58 | Male/Female | Median age at diagnosis in month | Median follow up duration in month |
|---|---|---|---|---|
| DRTA | 27 | 15/12 | 12(3-84) | 12(6-24) |
| Barter S | 16 | 10/6 | 12(6-60) | 12(7-36) |
| Gitleman S | 1 | 1/0 | 60 | 18 |
| Fanconi S | 6 | 3/3 | 17.5(3-60) | 12(9-13) |
| NDI | 3 | 2/1 | 60(29-84) | 12(7-12) |
| PRTA | 4 | 2/2 | 36(26-42) | 12(12-18) |
| RTA4 | 1 | 0/1 | 5 | 7 |

DRTA=distal renal tubular acidosis, NDI=nephrogenic diabetes insipidus, PRTA=proximal renal tubular acidosis, RTA4=renal tubular acidosis type 4

## Clinical presentation:

Failure to thrive was the most common presenting feature (91.4% of cases) followed by polydipsia(81%), delayed motor development(75.9%), dehydration episodes(72.4%), polyurea(70.72%), vomiting(65.5%), signs of rickets either clinically or radiologically or both(63.8%), weakness(56.9%), nephrocalcinosis(34.5%), seizures(24.1%), bone deformities with or without pathological fractures(17.2%). Deafness and photophobia were the least encountered (one case of DRTA had deafness and the case of cystinosis had photophobia).

Table: The main presenting features of renal tubular disorders

| Renal tubular disorder | Failure to thrive | Polyurea | Dehydration episodes | Nephrocalcinosis |
|---|---|---|---|---|
| DRTA (n=28) | 25 | 19 | 21 | 13 |
| Barter S (n=16) | 14 | 10 | 10 | 7 |
| Gitleman S (n=1) | 1 | 1 | 0 | 0 |
| Fanconi S (n=6) | 6 | 4 | 5 | 0 |
| PRTA (n=4) | 4 | 3 | 3 | 0 |
| NDI (n=3) | 2 | 3 | 2 | 0 |
| RTA4 (n=1) | 1 | 1 | 1 | 0 |

DRTA=distal renal tubular acidosis, NDI=nephrogenic diabetes insipidus, PRTA=proximal renal tubular acidosis, RTA4=renal tubular acidosis type 4

Consanguinity was noticed in 72.4% of cases (p value .001). 60% of cases have similar condition in their families. 29.3% of cases had low birth weight (birth

weight < 2.5 kg). Prematurity was noticed in 34.48% of cases. 60.34% of these children reported similar conditions among their relatives. 34.48% of cases had preterm labour (born before 37 weeks of gestation). 41.38% of cases needed neonatal intensive care admission for variety of reasons. Some of them were admitted due to persistent vomiting and dehydration episodes.

# Height outcome:

In patients with DRTA, a significant improvement in height was noticed (P value=0.005) thanks to proper management and follow up. Patients with Barter syndrome showed clinical improvement in height, but it was statistically not significant (P value=0.053). As regard patients with Fanconi syndrome, there was no height improvement. Patients with nephrogenic diabetes insipidus had clinical improvement in height, but not statistically significant (P value=0.109).Patients with proximal renal tubular acidosis showed no height improvement. In addition, there was a single case of Gitleman syndrome and another one of renal tubular acidosis type 4. They both showed height increase.

Table: Height outcome assessment

| Renal tubular disorder | Median Z score height at diagnosis | Median Z score height at follow up | P value |
|---|---|---|---|
| DRTA | -3.3 (-8 : 0.6) | -2 (-7.6 : 2.7) | .005 |
| Barter S | -2.3 (-5 : -0.9) | -2.15 (-3.8: 1.9) | .053 |
| Gitleman S | -2.4 | -2.3 | ---------- |
| Fanconi S | -4.6 (-7.5: -3.1) | -4.8 (-5.5 : -4.4) | .599 |
| NDI | -4 (-6.3 : 0) | -3.2 (-4.3 : 0.9) | .109 |
| PRTA | -3.9 (-4.5 : -3.7) | -4.15 (-4.4 : -2.8) | 1 |
| RTA4 | -4.2 | -3.2 | ---------- |

DRTA=distal renal tubular acidosis, NDI=nephrogenic diabetes insipidus, PRTA=proximal renal tubular acidosis, RTA4=renal tubular acidosis type 4

# Weight outcome:

Marked improvement in weight was noticed in patients with DRTA and barter syndrome (statistically and clinically significant). There was no weight improvement in patients with Fanconi syndrome. As regard to children with nephrogenic diabetes insipidus, clinical improvement in weight was noticed, but not statistically significant. Mild weight improvement was observed in children with PRTA. Catch up growth was seen in the child with Gitleman syndrome and the child with type 4 renal tubular acidosis.

| Renal tubular disorder | Median Z score weight at diagnosis | Median Z score weight at follow up | P value |
|---|---|---|---|
| DRTA | -4 (-6.6: -0.2) | -1.3 (-5.9: 3.3) | .000 |
| Barter S | -3.95 (-5.8: -1.9) | -0.7 (-3.4: -1.5) | .001 |
| Gitleman S | -4.8 | -3.5 | ------ |
| Fanconi S | -4.9 (-5.8: -3.3) | -4.9 (-5.5: -3.7) | .674 |
| NDI | -1.9 (-3.6: 4.7) | 1.4 (-.8: 4.5) | .285 |
| PRTA | -3.9 (-5.6: -3.3) | -3.45 (-5.3: -1.9) | .197 |
| RTA4 | -6.4 | -3.3 | ------ |

DRTA=distal renal tubular acidosis, NDI=nephrogenic diabetes insipidus, PRTA=proximal renal tubular acidosis, RTA4=renal tubular acidosis type 4

# Renal function outcome:

Only one case of Fanconi syndrome developed chronic renal failure and started renal replacement therapy. No significant change in glomerular filtration rate was noticed in all children.

| Renal tubular disorder | Median GFR at diagnosis | Median GFR at follow up | P value |
|---|---|---|---|

| | | | |
|---|---|---|---|
| DRTA | 65.7 (50-111) | 75.09 (43.21-122.31) | .075 |
| Barter S | 69.39 (42.57-118.74) | 74.72 (50.25-132.59) | .148 |
| Gitleman S | 68 | 94.16 | ----- |
| Fanconi S | 77.9 (54.14-118) | 89.28 (12.39-111.51) | .6 |
| NDI | 92.51 (67.23-113.58) | 79.16 (65.01-109.03) | .109 |
| PRTA | 60.73 (50.83-82.6) | 56.24 (51.63-80.1) | .465 |
| RTA4 | 58.85 | 66.87 | ----- |

GFR: glomerular filtration rate, DRTA=distal renal tubular acidosis, NDI=nephrogenic diabetes insipidus, PRTA=proximal renal tubular acidosis, RTA4=renal tubular acidosis type 4.

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