Pattern of hereditary renal tubular disorders in Egyptian children

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ABSTRACT

Background. Hereditary renal tubular disorders (HRTD) represent a group of genetic diseases characterized by disturbances in fluid, electrolyte, and acid-base homeostasis. There is a paucity of studies on pediatric HRTD in Egypt. In this study, we aimed to study the pattern, characteristics, and growth outcome of HRTD at an Egyptian medical center.

Methods. This study included children from one month to < 18-years of age with HRTD who were diagnosed and followed up at the Pediatric Nephrology Unit of Sohag University Hospital from January 2015 to December 2021. Data on patients’ demographics, clinical features, growth profiles, and laboratory characteristics were collected.

Results. Fifty-eight children (57% males; 72% parental consanguinity; 60% positive family history) were diagnosed with seven HRTD types. The most commonly encountered disorders were distal renal tubular acidosis (distal renal tubular acidosis [RTA] 27 cases, 46.6%) and Bartter syndrome (16 cases 27.6%). Other identified disorders were Fanconi syndrome (6 cases with cystinosis), isolated proximal RTA (4 cases), nephrogenic diabetes insipidus (3 cases), and one case for each RTA type IV and Gitelman syndrome. The median age at diagnosis was 17 months with a variable diagnostic delay. The most common presenting features were failure to thrive (91.4%), developmental delay (79.3%), and dehydration episodes (72.4%). Most children showed marked improvement in growth parameters in response to appropriate management, except for cases with Fanconi syndrome. Last, only one case (with cystinosis) developed end-stage kidney disease.

Conclusions. HRTD (most commonly distal RTA and Bartter syndrome) could be relatively common among Egyptian children, and the diagnosis seems challenging and often delayed.

Key words: renal tubular disorders, renal tubular acidosis, Bartter syndrome, failure to thrive, dehydration.
Egypt is one of the largest countries in the Middle East and Africa, spanning over one million Km² and has >100 million population. There is a paucity of studies on HRTD among children in Egypt and developing countries. Given the high rate of consanguineous marriage (up to 60%), the prevalence of HRTD may be relatively higher among Egyptian children. However, the diagnosis may be challenging due to the broad, nonspecific, and overlapping manifestations as well as poor pediatrician awareness and limited diagnostic capabilities. In this study, we aimed to study the pattern, relative frequency, characteristics, and outcome of hereditary renal tubular disorder at an Egyptian medical center.

Material and Methods

This study included children from one month to <18-years of age with hereditary renal tubular disorders who were diagnosed and followed up at the Pediatric Nephrology Unit of Sohag University Hospital (PNU-SUH) from January 2015 to December 2021. We excluded children with renal tubular disorders due to acquired causes, such as drugs (e.g., diuretics), intoxications (e.g., vitamin D), autoimmune disorders, and obstructive uropathy, as well as those with a follow-up duration of fewer than six months. The PNU-SUH has been established since 2005 as the main referral center for children with renal disorders in Sohag governorate, which is located in southern Egypt, spanning over 1,547 km², and has >5 million population. The present study was approved by the Medical Research Ethics Committee of Sohag Faculty of Medicine on April 11th, 2021 (IRB Registration Number: Soh-Med-21-04-04) and followed the ethical guidelines of the 1964 Declaration of Helsinki and its 2013 revision. Informed consent was obtained from parents or authorized legal guardians of children participating in this study.

Enrolled children underwent thorough history taking and physical examination, including patients’ demographics, perinatal history (e.g., polyhydramnios, prematurity, and admission to neonatal intensive care unit [NICU]), family history, age at presentation and diagnosis, and detailed manifestations (e.g., failure to thrive [FTT], delayed development, polyuria, polydipsia, episodes of dehydration, vomiting, seizures, rickets/bone deformities, photophobia, and deafness). Anthropometric measures and development were evaluated using WHO growth charts (percentiles and z-scores) and the Denver II developmental screening test (http://denverii.com), respectively. Laboratory investigations included complete blood count, hepatic and renal function tests, blood gases and anion gap estimation, serum levels of electrolytes, glucose, urine analysis and urinary chloride, sodium, anion gap, and calcium/creatinine ratio, estimation of glomerular filtration rate, renal Ultrasound, bone radiograph, bicarbonate loading test, and ammonium loading test as well as slit lamp examination for corneal cystine crystals. Following diagnosis, children received appropriate management according to guidelines with regular follow-up; data were obtained during serial follow-up visits.

Diagnosis of HRTA relied on characteristic clinical and biochemical data after exclusion of acquired causes. dRTA was diagnosed based on normal anion gap (hyperchloremic) metabolic acidosis, hypokalemia, inability to lower urinary pH below 5.5 during metabolic acidemia, and hypercalciuria. Isolated pRTA was diagnosed on the basis of hyperchloremic metabolic acidosis, no or mild hypokalemia, and preserved ability to lower urinary pH below 5.5 in the case of metabolic acidemia or acid loading. Fanconi syndrome was defined as pRTA with glucosuria, phosphaturia, and aminoaciduria. Cystinosis was defined as Fanconi syndrome with cystine crystals in the cornea and/or high cystine levels in leukocytes.

RTA type IV was diagnosed on the basis of hyperchloremic metabolic acidosis, hyperkalemia, and the ability to lower urinary pH below 5.5 in response to metabolic acidemia. Diagnosis of Bartter syndrome relied on a history of polyhydramnios/prematurity and hypochloremic hypokalemic metabolic
alkalosis with excessive urinary loss of calcium and chloride. Gitelman syndrome was defined as hyperchloremic metabolic alkalosis with hypocalciuria and hypomagnesemia. Nephrogenic diabetes insipidus (NDI) was diagnosed on the basis of polyuria, polydipsia, high plasma osmolarity concomitant with low urine osmolarity, persistent hypernatremia, high serum vasopressin, and no response to vasopressin test.\textsuperscript{1,3,10-15}

The estimated glomerular filtration rate (eGFR) was calculated using the revised Schwartz formula for pediatric patients.\textsuperscript{16} Chronic kidney disease (CKD) was defined according to Kidney Disease Improving Global Outcomes (KDIGO) criteria as permanent (> 3 months) eGFR < 60 ml/min/1.73 m\textsuperscript{2}.\textsuperscript{17}

**Statistical analysis**

Patient data were analyzed using IBM SPSS for Windows version 25 (IBM Corp., Armonk, NY, USA). Qualitative data were presented as frequency and percentages, and quantitative data were presented as medians and ranges (as the Shapiro-Wilk test showed that quantitative data were not normally distributed). We used Fisher exact test to compare frequencies of FTT and developmental delay between patients diagnosed during and after the first year of life. Height and weight measures were compared during follow-up using Wilcoxon test. A \( p \)-value (2-tailed) < 0.05 was considered statistically significant.

**Results**

Over seven years (2015 – 2021), 58 children (33 males and 25 females) from 54 unrelated families were diagnosed with HRTD at our medical center. One family had three siblings with Fanconi syndrome and two families each had two siblings with dRTA. Positive parental consanguinity and family history of similar conditions were present in 72.4% and 60.3% of cases, respectively. Nearly a third of cases (34.5%) were born prematurely (<37 weeks of gestational age), and 41.4% required NICU admission. The median age at diagnosis was 17 months (range 3 months to 7 years); around 45% of cases were diagnosed during the first year of life, while only two cases were diagnosed after the age of 6 years. The most commonly encountered disorders were dRTA (27 cases, 46.6%) and Bartter syndrome (16 cases, 27.6%). Other identified disorders were Fanconi syndrome (6 cases; all have cystinosis), isolated pRTA (4 cases), NDI (3 cases), and one case for each of RTA IV and Gitelman syndrome (Table I).

As shown in Table II, the most common presenting feature in children under study was FTT (91.4%), developmental delay (79.3%),

<table>
<thead>
<tr>
<th>Category</th>
<th>Patients' n (%)</th>
<th>Male/Female</th>
<th>Consang., n (%)</th>
<th>Family history, n (%)</th>
<th>Age at diagnosis (months), median (IQR)</th>
<th>Follow-up duration (months), median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dRTA</td>
<td>27 (46.6)</td>
<td>15/12</td>
<td>19 (70.4)</td>
<td>14 (51.9)</td>
<td>12 (6-24)</td>
<td>12 (12-12)</td>
</tr>
<tr>
<td>Bartter syndrome</td>
<td>16 (27.6)</td>
<td>10/6</td>
<td>10 (62.5)</td>
<td>10 (62.5)</td>
<td>12 (7-31)</td>
<td>12 (10.5-12)</td>
</tr>
<tr>
<td>Fanconi syndrome</td>
<td>6 (10.3)</td>
<td>3/3</td>
<td>6 (100)</td>
<td>5 (83.3)</td>
<td>17.5 (12-48)</td>
<td>12 (12-12)</td>
</tr>
<tr>
<td>pRTA</td>
<td>4 (6.9)</td>
<td>2/2</td>
<td>3 (75)</td>
<td>2 (50)</td>
<td>36 (31-39)</td>
<td>12 (12-15)</td>
</tr>
<tr>
<td>NDI</td>
<td>3 (5.2)</td>
<td>2/1</td>
<td>2 (66.7)</td>
<td>2 (66.7)</td>
<td>60 (29-84)</td>
<td>12 (7-12)</td>
</tr>
<tr>
<td>Gitelman syndrome</td>
<td>1 (1.7)</td>
<td>1/0</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>60</td>
<td>36</td>
</tr>
<tr>
<td>RTA IV</td>
<td>1 (1.7)</td>
<td>0/1</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>33/25</td>
<td>42 (72.4)</td>
<td>35 (60.3)</td>
<td>17 (7-36)</td>
<td>12 (12-12)</td>
</tr>
</tbody>
</table>

\( dRTA \): distal renal tubular acidosis, \( NDI \): nephrogenic diabetes insipidus, \( pRTA \): proximal renal tubular acidosis, \( RTA IV \): renal tubular acidosis type IV
### Table II. Main presenting features in children with renal tubular disorders.

<table>
<thead>
<tr>
<th>Category</th>
<th>Failure to thrive</th>
<th>Developmental delay</th>
<th>Dehydration episodes</th>
<th>Polyuria</th>
<th>Vomiting</th>
<th>Rickets</th>
<th>Skeletal deformity/fracture</th>
<th>Nephrocalcinosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>dRTA (n=27)</td>
<td>25 (92.6)</td>
<td>23 (85.2)</td>
<td>21 (77.8)</td>
<td>19 (70.4)</td>
<td>18 (66.7)</td>
<td>17 (63)</td>
<td>2 (7.4)</td>
<td>13 (48.2)</td>
</tr>
<tr>
<td>Bartter syndrome (n=16)</td>
<td>14 (87.5)</td>
<td>12 (75)</td>
<td>10 (62.5)</td>
<td>10 (62.5)</td>
<td>9 (56.3)</td>
<td>10 (62.5)</td>
<td>0</td>
<td>7 (43.8)</td>
</tr>
<tr>
<td>Fanconi syndrome (n=6)</td>
<td>6 (100)</td>
<td>5 (83.3)</td>
<td>5 (83.3)</td>
<td>4 (66.7)</td>
<td>5 (83.3)</td>
<td>4 (66.7)</td>
<td>4 (66.7)</td>
<td>0</td>
</tr>
<tr>
<td>pRTA (n=4)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>3 (75)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>3 (75)</td>
<td>0</td>
</tr>
<tr>
<td>NDI (n=3)</td>
<td>2 (66.7)</td>
<td>0</td>
<td>2 (66.7)</td>
<td>3 (100)</td>
<td>1 (33.3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gitelman syndrome (n=1)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0</td>
<td>1 (100)</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0</td>
</tr>
<tr>
<td>RTA IV (n=1)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total (n=58)</strong></td>
<td>53 (91.4%)</td>
<td>46 (79.3%)</td>
<td>42 (72.4%)</td>
<td>41 (70.7%)</td>
<td>38 (65.5%)</td>
<td>37 (63.8%)</td>
<td>10 (17.2)</td>
<td>20 (34.5%)</td>
</tr>
</tbody>
</table>

Data are described as n (%)

dRTA: distal renal tubular acidosis, NDI: nephrogenic diabetes insipidus, pRTA: proximal renal tubular acidosis, RTA IV: renal tubular acidosis type IV

### Table III. Height and weight outcome assessment.

<table>
<thead>
<tr>
<th>Category</th>
<th>Age at diagnosis (months), median (IQR)</th>
<th>Age at last follow-up (months), median (IQR)</th>
<th>Height Z-score at diagnosis, median (IQR)</th>
<th>Height Z-score at follow-up, median (IQR)</th>
<th>p-value*</th>
<th>Weight Z-score at diagnosis, median (IQR)</th>
<th>Weight Z-score at follow-up, median (IQR)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>dRTA (n = 27)</td>
<td>12 (6-24)</td>
<td>24 (17-36)</td>
<td>-3.3 (-5.5, 0.2)</td>
<td>-2 (-3.8 : -1)</td>
<td>0.005</td>
<td>-4 (-5.4, -2.9)</td>
<td>-1.3 (-2.1, 0.3)</td>
<td>0.000</td>
</tr>
<tr>
<td>Bartter syndrome (n = 16)</td>
<td>12 (7-31)</td>
<td>23 (18-48)</td>
<td>-2.3 (-3.1, -1.6)</td>
<td>-2.15 (-3.2, -1.4)</td>
<td>0.053</td>
<td>-3.9 (-5.1, -3)</td>
<td>-0.7 (-2.1, 0.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fanconi syndrome (n = 6)</td>
<td>17.5 (12-48)</td>
<td>30 (24-60)</td>
<td>-4.6 (-5.3, -4.1)</td>
<td>-4.8 (-5.3, -4.5)</td>
<td>0.599</td>
<td>-4.9 (-5.7, -4.2)</td>
<td>-4.9 (-5.2, -3.8)</td>
<td>0.674</td>
</tr>
<tr>
<td>pRTA (n = 4)</td>
<td>36 (31-39)</td>
<td>48 (43-54)</td>
<td>-3.9</td>
<td>-4.15</td>
<td>NA</td>
<td>-3.9</td>
<td>-3.45</td>
<td>NA</td>
</tr>
<tr>
<td>NDI (n = 3)</td>
<td>60 (29-84)</td>
<td>72 (36-96)</td>
<td>-4</td>
<td>-3.2</td>
<td>NA</td>
<td>-1.9</td>
<td>1.4</td>
<td>NA</td>
</tr>
<tr>
<td>Gitelman syndrome (n = 1)</td>
<td>60</td>
<td>96</td>
<td>-2.4</td>
<td>-2.3</td>
<td>NA</td>
<td>-4.8</td>
<td>-3.5</td>
<td>NA</td>
</tr>
<tr>
<td>RTA IV (n = 1)</td>
<td>5</td>
<td>12</td>
<td>-3.9</td>
<td>-4.15</td>
<td>NA</td>
<td>-6.4</td>
<td>-3.3</td>
<td>NA</td>
</tr>
</tbody>
</table>

dRTA: distal renal tubular acidosis, NA: not applicable, NDI: nephrogenic diabetes insipidus, pRTA: proximal renal tubular acidosis, RTA IV: renal tubular acidosis type IV

*Wilcoxon test
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and dehydration episodes (72.4%). Compared with patients diagnosed in the first year of life, those diagnosed after the first year of life had higher proportions of FTT (100% vs. 80.8%, \( p = 0.014 \)) and developmental delay (87.5% vs. 69.2%, \( p = 0.111 \)). Other features included polyuria (70.7%), vomiting (65.5%), clinical and/or radiological signs of rickets (63.8%), nephrocalcinosis (34.5%), seizures (24.1%), and bone deformities with or without pathological fractures (17.2%). Hearing impairment and photophobia was identified in only one case with dRTA and cystinosis, respectively.

The assessment of height and weight outcomes is provided in Table III and Fig. 1A & 1B. Patients with dRTA showed statistically significant improvements in both height and weight. Patients with Bartter syndrome had improvements in both height and weight, but only weight improvement reached a statistically significant level. Other disorders showed no statistically significant difference in height and weight during the follow-up.

Our PNU-SUH follow recommended dietary and pharmacological guidelines in management of fluids, electrolytes, acid-base, and other disorders in children with HRTD.\(^3\)\(^,\)\(^4\)\(^,\)\(^5\) However, access to medical services and medication as well as in-adherence to treatment were major challenges. Acid-base and electrolyte homeostasis could not be normalized in some cases, particularly those with pRTA and Fanconi syndrome. During the study duration, children under study had no significant changes in GFR, and only one case with cystinosis developed CRF and started renal replacement therapy.

### Discussion

Renal tubules play a crucial role in fluids, electrolytes, and acid-base homeostasis. Tubular dysfunction can result from a variety of hereditary and acquired causes and has to be considered in the differential diagnosis of children with failure to thrive, polyuria, refractory rickets, hypokalemia, and metabolic acidosis.\(^3\) The present study investigated the pattern, characteristics, and outcome of 58 children with HRTD at an Egyptian medical center. These data advance our knowledge on HRTD in southern Egypt and are quite important for increasing pediatricians’ awareness for early diagnosis and treatment, which is essential for a better outcome.

In the present study, the most commonly identified HRTD were dRTA and Bartter syndrome, which is consistent with some previous studies. For instance, dRTA and Bartter syndrome were the most frequent disorders in two Indian studies on children with HRTD.\(^18\)\(^,\)\(^19\) A Turkish study on 226 patients with HRTD reported that the most common types

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**Fig. 1.** A. Height z-scores at diagnosis and follow-up. B. Weight z-scores at diagnosis and follow-up

dRTA: distal renal tubular acidosis, NDI: nephrogenic diabetes insipidus, pRTA: proximal renal tubular acidosis, RTA IV: renal tubular acidosis type IV
were dRTA (45.6%), pRTA (26.6%), and Bartter syndrome (21.7%). Based on the data of more than 200 patients mostly from Latin America and Spain, the Renal Tube Network reported that the most frequent tubulopathies are dRTA and Bartter syndrome.

On the other hand, a German study reported that nephropathic cystinosis, XLHR, and idiopathic hypercalciuria are the most frequent HRTD. In a Spanish study, Gitelman syndrome was the most common HRTD (36%), followed by dRTA (15%) and cystinosis (17%).

Idiopathic hypercalciuria (35%), followed by cystinosis and RTA (each 21.6%) were the most frequent HRTD among 37 children from Iraq. Another Iraqi study on 80 patients reported that pRTA (56.3%), dRTA (30%), and Bartter syndrome (10%) are the most frequent HRTD. In an Iranian study, the most commonly reported tubulopathies were RTA (33%), calcium disorders (27%), and cystic diseases (17%). Our study didn't include certain types of HRTD, such as idiopathic hypercalciuria, which may be related to a referral bias, since most of these children may not be referred to a pediatric nephrology center.

The variability in the pattern and relative frequency of HRTD among studies can be attributed to a variety of reasons. First, true differences in birth prevalence of HRTD may occur among certain populations. Second, studies have different inclusion and exclusion criteria. For example, Hooman et al. included both hereditary and acquired tubulopathies, while Topaloglu et al. and Azat studies excluded patients with NDI, idiopathic hypercalciuria, cystinuria, and stone diseases such as hyperoxaluria. Third, there are differences in the level of physician awareness and available diagnostic facilities, which may preclude diagnosis of certain HRTD in resource-limited areas. Last, most studies have a small sample size, which may not properly reflect the real pattern of HRTD.

Children in our study were diagnosed at a median age of 17 months with a range from three months to seven years. This is close to Kiran et al. study, in which the median age at diagnosis was 18 months. Some studies reported an earlier median age at diagnosis, such as 12 months in the Azat study, while other studies reported later diagnosis, such as four years in Sinha et al. study and five years in Blázquez Gómez et al. study. It is important to note that patients with more severe disorders, such as dRTA, Bartter, and Fanconi syndrome, were diagnosed at an earlier age than that of patients with disorders of more silent course, such as Gitelman syndrome. Moreover, there was a notable delay between the onset of symptoms and diagnosis, which has been also reported in some previous studies, particularly in developing countries.

The diagnostic delay could be attributed to a delay in seeking medical advice, heterogenous clinical manifestations, improper physicians’ awareness, and limited diagnostic facilities. Indeed, a survey study of attendees to the Spanish Nephrology Society Congress in 2019 revealed inadequate knowledge on dRTA.

The general percentage of consanguineous marriage in Egypt is 35%, but it reaches 60% in rural areas. In the present study, positive parental consanguinity and family history of similar conditions were present in 72.4% and 60.3%, respectively, of children with HRTD. A high proportion of consanguinity has been reported in previous studies from the Middle East, such as 77% in Topaloglu et al., and 85% in Azat and a high proportion of other affected family members have been reported, such as 58.8% in Azat’s study. The high proportions of consanguinity and other affected family members indicate a high incidence of HRTD in Egypt. When this is combined with the observed diagnostic delay, it is highly likely that many other patients with HRTD remain undiagnosed. This also underscores the importance of screening other family members after confirming the diagnosis of the index patient, which may identify other patients so that management can be started early to prevent possible acute and long-term complications.
The most common presenting manifestation in children under study was FTT (91.4%), followed by developmental delay (79.3%) and dehydration episodes (72.4%). Likewise, FTT was the most frequent presenting feature in some previous studies.\textsuperscript{1,18,23} Therefore, tubular disorders should be considered as an important differential diagnosis in all children with FTT. The high percentage of FTT may indicate delayed diagnosis. Indeed, we found that diagnosis after the first year of life is significantly associated with having FTT, which underscores the importance of early diagnosis. FTT in children with HRTD may be explained by multiple factors, including loss of nutrients, anorexia and vomiting, dehydration, chronic acidosis or alkalosis, chronic hypokalemia, and/or CKD.\textsuperscript{4-6,8} As shown in our study, most children with FTT showed marked improvement in height and weight parameters in response to appropriate management, except for cases with Fanconi syndrome, which goes in line with previous studies.\textsuperscript{4,18}

Nearly a third of children with HRTD in our study had nephrocalcinosis. Nephrocalcinosis is one of the common manifestations of HRTD, particularly dRTA and Bartter syndrome, which could be attributed to the alkaline urine and hypercalciuria, predisposing to calcium precipitation and stone formation.\textsuperscript{22,24} Only one case (with cystinosis) developed CKD and started renal replacement therapy. Nephropathic cystinosis has been reported as the leading cause of CKD in previous studies.\textsuperscript{1,18} The percentage of CKD in our study is quite lower than previous studies, such as 42% in Haffner et al.\textsuperscript{21}, 31% in Blázquez Gómez et al.\textsuperscript{4}, and 16. 2% in Al Mosawi.\textsuperscript{22}, which may be related to the shorter follow-up duration.

Patients under study were managed at PNU-SUH, which follows updated recommendations for management of HRTD. However, some patients had restricted access to certain medical services and medications due to economic constraints. Furthermore, other patients showed in-adherence to medications and irregular follow-up. The limited access to medication and patients’ in-adherence to treatment coupled with delayed diagnosis represent major challenges to the proper management of children with HRTD in Egypt as well as other developing countries.\textsuperscript{1,18,23}

The strengths of the present study include the first description of pediatric HRTD in Egypt, relying on characteristic criteria for diagnosis of different entities of HRTD, and the follow-up of children with HRTD for changes in weight and height z-scores. Nevertheless, our study has some limitations, first, it is a single-center study with relatively small sample size, which limit the generalizability of findings. However, HRTD are rare, and patients in this study were collected over seven years. Larger multicenter studies are recommended in areas with limited data on HRTD, including Egypt and other developing countries. Second, patients included in this study were referred to our pediatric nephrology center, and it is highly likely that other patients, particularly those with milder manifestations, were not recognized or referred by their physicians. Third, not all patients under study underwent comprehensive and repeated audiological assessment, which is important for early detection of hearing defects associated with certain HRTD. Last, diagnosis of HRTD relied on characteristic clinical and biochemical features, but without genetic confirmation. It would be important to study the molecular basis of HRTD among Egyptian children in future studies.

Over seven years, we identified 58 children with HRTD. The most common disorders were dRTA and Bartter syndrome, and the most common presenting manifestations were FTT, developmental delay, and dehydration episodes. Most children had improved growth with appropriate management and had preserved renal function. These data improve our knowledge on HRTD in southern Egypt and are crucial for increasing pediatrician awareness for appropriate management, which is essential for better outcome.
Acknowledgement

The authors thank all physicians at the Pediatric Nephrology Unit – Sohag University Hospital for their dedicated medical care of children with hereditary renal tubular disorders.

Ethical approval

The present study was approved by the Medical Research Ethics Committee of Sohag Faculty of Medicine on April 11th, 2021 (IRB Registration Number: Soh-Med-21-04-04) and followed the ethical guidelines of the 1964 Declaration of Helsinki and its 2013 revision. Informed consent was obtained from parents or authorized legal guardians of children participated in this study.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: MMA, MK; data collection: MAMO, GABA, EA, MK; analysis and interpretation of results: MAMO, EA; draft manuscript preparation: MAMO, EA. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES


