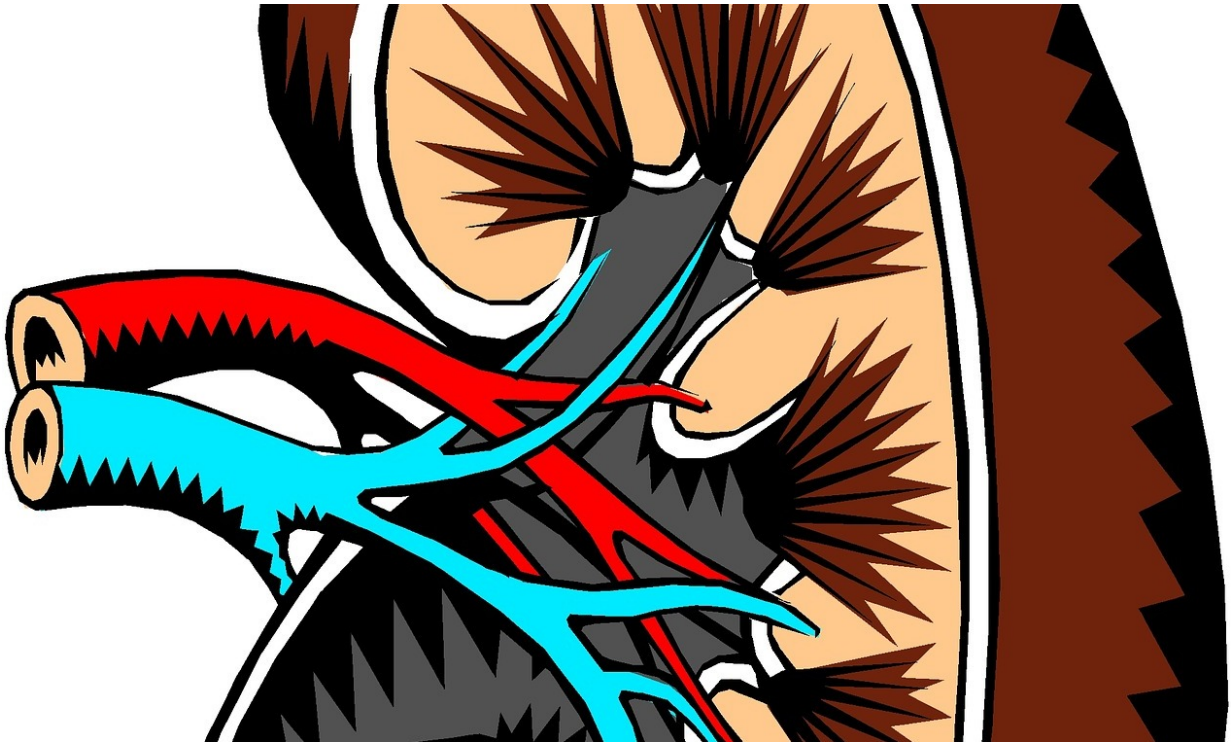
Researchers report new findings on familial primary distal renal tubular acidosis

February 20 2019



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In addition to regulating the body's fluid balance by excreting greater or smaller amounts of urine, the kidneys also maintain the proper balance of electrolytes (salts) and the pH (an acid-base equilibrium) of the body. Excess acid is secreted into the urine by healthy kidneys. This process takes place in a specific part of the kidney, the distal tubules. When this

excretion of acid is disturbed, the concentration of acid in the body increases, resulting in a disorder called distal renal tubular acidosis (dRTA).

"Too much acid in our bodies has a lot of negative effects," explains Prof. Dr. Detlef Bockenhauer, London. "In the first instance, the acid dissolves the bones, leading to complications such as rickets. And the calcium released from the bone ends up in the urine, where it can cause kidney stones."

Distal renal tubular acidosis is a rare disease affecting only about one in 100,000 people, and is congenital in most cases—this is called familial or primary dRTA. Mutations in six genes have been identified that can cause the disorder. Symptoms may include large volumes of urine, thirst, fatigue, growth disorders and failure to thrive, bone damage (similar to rickets or osteoporosis) or kidney stones. Recurrent kidney stones or severe calcification of kidney tissue (nephrocalcinosis) may lead to progressive chronic kidney disease. A marked deficiency of serum potassium can be another complication, which can lead to paralysis, cardiac arrhythmia and, ultimately, death. Some inherited forms also lead to progressive deafness. Symptoms may vary considerably for the various gene mutations, with some patients remaining asymptomatic and the diagnosis is made only incidentally.

Treatment involves administering alkali supplements (acid binders such as bicarbonate or citrate) on a daily basis for life.

"Because the disease is so rare, there are no major long-term studies of its progression and prognosis, which makes it more difficult to manage it medically and to properly inform parents and patients," explains Prof. Bockenhauer. For these reasons, the aim of the multinational initiative was to clarify a number of unresolved questions to improve the diagnosis, therapy and handling of the disease for physicians, patients

and parents. Paediatric and adult nephrologists contributed to the study, and all available data (demographic, biochemical, genetic and clinical) were collected using online forms.

The results of the study have now been released. Data on 340 patients from 29 countries were collected (52 percent female). The median age of patients was 11 years (0-70), 83 patients (24 percent) were adults (18 years). The median presentation age was 0.5 years (range 0-54) and 11 years at last follow-up (0-70). Mutation analyses were performed in 206 of the patients (61 percent); gene mutations were identified in 170 of that group (83 percent). The adult patients had reached heights slightly below average (with a standard deviation score (SDS) of -0.57). The prevalence of stage 2 chronic kidney disease (CKD) was 35 percent among children and 82 percent among adults.

Calcification of kidney tissue (nephrocalcinosis) was reported in 88 percent of patients. Kidney stones (nephrolithiasis) were most common in cases with SLC4A1 mutations (42 percent vs. 21 percent). 36 percent had hearing loss (most frequently in cases with ATP6V1B1 mutations). Adequate therapy with a normal acid-base balance and without excess urinary calcium loss was achieved in only 158 patients (51 percent) -predominantly in countries with a high gross domestic product. Importantly, when analysing the data from adult patients, the researchers noted that those with adequate treatment had a better final height and better kidney function, compared to those, in whom adequate buffering of acid was not achieved. "This is an important message to all clinicians taking care of these patients: we really must make sure to control the disease as effectively as possible so that our patients can reach their full growth potential and maintain overall kidney function."

"All in all, the progression and outcome of distal renal tubular acidosis in this large cohort of patients can be considered favourable," Prof. Bockenhauer summarises. "Most patients reach an adult height in the

normal range, and no patient had severe chronic kidney disease (stage 5 CKD) or needed dialysis. Nevertheless—82 percent of the patients reached stage 2-4 CKD; this is likely attributable to the fact that optimal management of acid-base balance was achieved in only about half the patients. Future efforts must now concentrate on establishing the best possible management of treatment for all patients in all countries."

More information: Sergio Camilo Lopez-Garcia et al, Treatment and long-term outcome in primary distal renal tubular acidosis, *Nephrology Dialysis Transplantation* (2018). DOI: 10.1093/ndt/gfy409

Provided by ERA-EDTA