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# A review on renal tubular acidosis

*Nirmay Sonar*
*nirmay9833@gmail.com*
*Independent Researcher*

*Iftikar Khadas*
*khadas56@gmail.com*
*Independent Researcher*

## ABSTRACT

**A rare renal condition, a known cause, but the lesser-known cause of Metabolic Acidosis, is Renal Tubular Acidosis. Renal Tubular Acidosis, or RTA as abbreviated, is due to mechanisms that dismantle the balance of Hydrogen and Bicarbonate in the blood-urine axis, leading to a lower pH, or acidic blood, as well as a vast array of complications associated with it. History dates the first indexed appearance to Lightwood in 1935, and Butler et al in children. About a decade later, in 1945, Baines et.al described it in adults. This review article looks at the literature and provides a brief insight into the topic.**

***Keywords***: *Nephrology, RTA, Renal Tubular Acidosis, Medicine, Harrison, Renal, Kidney*

## 1. INTRODUCTION

Renal Tubular Acidosis, or RTA as it is abbreviated, is an acidosis of renal origin. As the name suggests, it is systemic acidosis, or metabolic acidosis due to an inability of the kidneys to excrete acid in the urine [10]. The normal renal function, of maintaining acid-base balance, between the filtrate and blood, is hampered. There are four known types of RTA, each a result of a lesion at a varied point in the microstructure of the nephron.

### Epidemiology

This condition is rare, each type exhibiting their specific etiology. Distal RTA may be seen in 1 in 10,000 individuals [1], whereas other variants are rare. Most cases present at infancy, with no sex predisposition.

### Pathophysiology

There are three basic mechanisms in the pathogenesis of RTA, the end-point of each being the presence of more protons (basically Hydrogen ions) in the blood.

An impaired hydrogen (acid ion) secretion in the late distal collecting tubule (DCT) or cortical collecting duct (CT);
Decreased bicarbonate (base ion) reabsorption in the proximal collecting tubule (PCT);
Decreased Sodium (Na) reabsorption in the DCT or CT. A decreased sodium, translates to decreased potassium and hydrogen ions, due to the action of potassium hydrogen (K-H) ATPase transporter.

Type 1 or Distal Renal Tubular Acidosis
This is the commonest type of RTA, and as the name suggests, involves the DCT, and CT system.
The causes of Type 1 RTA can be divided as,

| Primary | Secondary |
|---|---|
| Idiopathic | Nephrocalcinosis |
| Hereditary | Chronic Urinary tract obstruction |
| Genetic mutations of Hydrogen pumps | Hypergammaglobulinemia |
| Genetic mutation of Bicarbonate pump | Lithium and Amphotericin B |

 

| Primary | Secondary |
|---|---|
| | Rejected Renal transplant |
| | Autoimmunity in form of Sjogren's |
| | Cirrhosis |

The basic mechanism in this case is failure of hydrogen secretion in distal tubule, where the alpha-intercalated cells in DCT and CT do not excrete protons, which leads to acidosis, and urine becomes alkaline as bicarbonate is excreted, thus raising the pH of the urine. With low hydrogen in urine, less ammonia is formed, and alkaline urine favours the precipitation of calcium phosphate as a renal calculi. High urinary calcium is seen as phosphate ions remain free in the urinary system, and binding with free calcium leads to devastating effects such as Nephrocalcinosis. [7][3] Since calcium gets depleted in this process, it is not uncommon to see Rickets in children, and Osteomalacia in adults.

A diagnosis can be made by urinary pH being more than 5.5 [3], with evidence of systemic acidosis. Plasma bicarbonate is decreased, from 30mEq/L to 23mEq/L. [2] Acid Load Test is a test in which we orally give ammonium chloride (100mg/kg) and check pH of urine hourly and plasma bicarbonate per 3 hours.

A definite diagnosis can be made by urinary pH and plasma bicarbonate.
Treatment follows three protocols:
1. Correct acidosis by oral sodium bicarbonate or sodium citrate, these are systemic alkalizers, and the dosage of sod. Bicarbonate is 1-4 mEq/kg of body weight.
2. Correct Hypokalemia by Potassium citrate.
3. Thiazide diuretic, which causes volume contraction, and increased proximal bicarbonate reabsorption.

**Type 2 RTA or Proximal Tubular Acidosis**
This type of RTA is a very rare type, and is due to the failure of brush border cells of the PCT to reabsorb bicarbonate, leading to loss of bicarbonate in urine. Thus, the mechanism of acidosis is not an increased proton concentration, but rather, an absence of bicarbonate to counter the acid ion.
The causes of type 2 RTA can be classified similarly,

| Primary | Secondary |
|---|---|
| Inherited | Amyloidosis |
| Genetic Mutation of Na-HCO3 transporter | Wilson's Disease [6] |
| | Heavy Metal toxicity |
| | Hyperparathyroidism |
| | Anti retrovirals |
| | Paraproteinemias |

The acidosis observed here is less severe as compared to type 1, hypokalemia and bone changes also follow. It is to be noted that type 2 RTA is commonly associated with Fanconi Syndrome, a syndrome leading to urinary wasting of glucose, phosphates, amino acids, uric acid, and proteins. [3]

Diagnosis is made on the fact that urinary pH will not go lower than 5.5 [8][3], as the constant bicarbonate excretion renders the urine basic. Additionally, plasma bicarbonate comparison and bone demineralization should be checked.

The treatment follows the principles of
1. Correct bicarbonate's urinary loss by giving large doses of sodium bicarbonate.
2. Correct loss of potassium by potassium supplements.
3. Thiazides

**Type 3 RTA**
No special name this time, Type RTA is considered to be a combination of Type 1 and Type 2, meaning defect in proximal and distal systems.
Causes of type 3 are not well known[5], but some have attributed this to a genetic mutation in Carbonic Anhydrase Type 2 enzyme, as it resides in both the PCT, and DCT.
Some notable features are osteopetrosis, cerebral calcifications, and mental retardation. [4]

 

**Type 4 RTA or Hyporeninemic Hypoaldosteroneism**
Sometimes also referred to as Hypokalemic Acidosis, as the name suggests, there is a deficiency of renin, aldosterone, or a resistance to aldosterone action.[5] For this variant of RTA, we come back to the DCT and CT, where there is maximum action of the Renin-Angiotensin-Aldosterone axis.

The causes of type 4 RTA are as follows, either due to a primary or secondary mineralocorticoid deficiency.

| Primary | Secondary |
|---|---|
| Destruction of Juxtaglomerular cells | Diabetes Mellitus |
| Decreased sympathetic drive, which innervates JG cells | Tubulointerstital nephritis |
| Decreased production of prostacyclins, which cause decrease in renin | Effects of NSAIDs |
| Primary Hypoaldosteronism or Addison's Disease | Severe Hypovolemia |
| ENAC gene mutation | Systemic Lupus Erythromatosus |

Whether it be decreased synthesis, or a resistance to Aldosterone, the effect is a decreased function of Na-K ATPase, leading to fall in sodium in blood, and rise in potassium in blood, and with that an increase in Hydrogen ion in blood. This becomes the only variant of RTA with Hyperkalemia[5]. Other features include hyperchloremia, reduced plasma bicarbonate.

Investigations reveal hyperkalemia, plasma changes, a normal ACTH stimulation test, low basal 24-hour urinary aldosterone, and response of plasma renin and plasma aldosterone falls.

Treatment is based on the severity of hyperkalemia, and includes [9]
1. Correction of Hyperkalemia by Fludrocortisone, bicarbonate, diuretics, or ion exchange, or a combination.
2. Correction of Hypoaldosteroneism by a mineralocorticoid like fludrocortisone, with addition of a glucocorticoid, if deficient.

## 2. CLINICAL FEATURES

Generally, the patient will not have any signs specific to the disease. Vague symptoms like decreased appetite, nausea, vomiting, abdominal pain can be seen.

The patient, on examination may be tachypneic, tachycardic, and hypotensive, suggesting that the acidosis has lead to systemic vasodilation, and proceeding to shock. Respiratory compensation, in form of Kussmaul respiration me be present, an effort to counter the metabolic acidosis by respiratory carbon dioxide washout (Respiratory Alkalosis).
It is possible in some cases, that the patient may develop renal calculi, especially in type 1, which will present characteristically, and advocate investigations for a renal cause.

## 3. CONCLUSION

To conclude this, RTA encompasses a wide spectrum of Medical Disciplines, ranging from Physiology and its changes, i.e Pathology, to Nephrology, Pediatrics, Immunology, Hematology, and Orthopedics. A small change in the transporters, the enzymes, or changes due to systemic disease inter-link this topic to many other systems, leading to the manifestations of RTA. Even though rare, with the commonest variant having an incidence of 1 in 10,000 individuals, the diagnosis and management poses to be quite a challenge.

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